Harvard Library

VOLUME 29 [illegible] 3

ARCHIVES
OF
DERMATOLOGY AND SYPHILOLOGY

EDITORIAL BOARD

WILLIAM ALLEN PUSEY, Chicago
MARTIN E. ENGMAN, St. Louis
REED D. [illegible]
WILLIAM T. CORLETT, Cleveland
GEORGE M. [illegible]
[illegible] J. WHITE, Boston

MARCH, 1934

PUBLISHED MONTHLY BY AMERICAN MEDICAL ASSOCIATION
DEARBORN STREET, CHICAGO, ILLINOIS. ANNUAL SUBSCRIPTION

Entered as Second-Class Matter, October 20, 1917, at the Postoffice at Chicago, Illinois, under the Act of Congress of March 3, 1879. Acceptance for mailing at special rate of postage provided for in Section 1103, Act of October 3, 1917, authorized [illegible]

CONTENTS OF THIS NUMBER

FEBRUARY, 1934 NUMBER 2

Treatment of Pneumococcic Septicemia. Louis W. Sauer, M.D., Detroit.

Studies on Granuloma Annulare and Special Reference to the Tuberculosis Theory. Jeffrey C. Michael, M.D., Houston, Texas.

Parapharmacologic Test in Dermatology: Further Studies and Some Critical Examinations. Isaac Ruth Falk, M.D., and David E. Mackh, M.D., Baltimore.

Multiple Benign Tumor-Like New Growths of the Sclerotic Type: Report of a Case. Norman Tobias, M.D., St. Louis.

Recurrent Fever and Phlebothrombosis Irradiation: A Corrective Factor in Certain Diseases of the Skin. Paul E. Becker, M.D., New York.

Blood Lipids in Xanthoma. Jeffrey C. Michael, M.D., and B. G. Nicholas, Ph.D., Houston, Texas.

"Consecutive" Dermatomyositis. Henry D. Rubin, M.D., New York.

Tuberculoderma of the Face. K. M. Michelsen, M.D., and L. E. Viner, M.D., Minneapolis.

Roentgen Therapy for Pain: A Consideration of the Indications, Technic and Treatment with Radiation. C. E. Lattimer, M.D., San Antonio, Texas.

Granuloma Venereum: Report of an Extensive Case. H. F. E. Wallhausen, M.D., and Andrew Wallhausen, Manila, P. I.

Hidradenoma Papilliferum. John A. Hartzell, M.D., Cleveland.

Adrenal Cortical Secretion of Stimulating Hormone. H. L. Hamblin, M.D., H. G. Mehrtens, M.D., and J. Spaulding, A.M., San Francisco.

Reviews and Comments.

Abstracts from Current Literature.

Society Transactions.

California Dermatological Society.

Chicago Dermatological Society.

Boston Dermatological Society.

Book Reviews.

Directory of Dermatologic Societies.

Copyright, 1934, by The American Medical Association

Archives of Dermatology and Syphilology

VOLUME 29 MARCH, 1934 NUMBER 3

CUTANEOUS MANIFESTATIONS OF ALLERGY

CHARLES MALLORY WILLIAMS, M.D.
Attending Dermatologist, Stuyvesant Square Hospital
NEW YORK

When a guinea-pig is treated parenterally with a small dose of any foreign serum, and then, after a period of incubation, receives a second dose of the same serum well below the amount necessary to produce symptoms in a normal animal, this second dose will be followed by severe symptoms, even by death. This increased sensitivity is called anaphylaxis. The casual reader is apt to interpret this statement of the facts as equivalent to saying that a dose of serum sensitizes an animal so that a second dose causes severe symptoms; but the two statements are not identical, and the second statement is not necessarily true, for it omits the essential details. The first sentence states that the animal used is the guinea-pig—an important detail, for some animals are less easily sensitized than others, and some only with great difficulty; white rats, for instance, can be sensitized only when the diet has been restricted to bread and water for some time [1] or when the suprarenal glands have been removed.[2] A small dose sensitizes more quickly than a large one, and in any case an incubation period must elapse. The second dose must be of appreciable size, and should be given intraperitoneally, or better, intravenously. If given subcutaneously, it may fail to produce a reaction. Not only do different species differ in their susceptibility to sensitization, but the symptoms differ widely. The guinea-pig is killed by contraction of the smooth muscles of the bronchi, the lungs at death being fixed in distention, while the pulmonary artery is permeable and the blood pressure within it is low. In the anaphylactic rabbit, the pulmonary artery is so contracted that it is impossible to force fluid through it. In the sensitized dog, the liver is stimulated to the production of smooth muscle-relaxing substances, which produce all the symptoms.[3] Each species reacts to this experiment in its own specific manner,

Read at the Fifty-Sixth Annual Meeting of the American Dermatological Association, Inc., Chicago, June 8, 1933.

1. Seegal, Beatrice C., and Korazo, Deborah: Anaphylaxis in the White Rat as Influenced by Diet, Arch. Path. **7**:827 (May) 1929.

2. Flashman, D. H.: The Effect of Suprarenalectomy on Active Anaphylactic Shock in White Rats, J. Infect. Dis. **38**:461, 1926.

3. Manwaring, W. H.: Anaphylatic and Immune Reactions, J. Immunol. **2**:517, 1917.

and within the species there are great individual differences. In all cases, however, new substances called antibodies appear in the blood stream, as is shown by the passive sensitization of a guinea-pig by injection into its circulation of blood from an actively sensitized guinea-pig, and the symptoms are produced by the action, usually on smooth muscle fiber, of yet another substance produced by the interaction of the fresh dose of serum and these antibodies. This particular type of allergy has been carefully studied, and has colored subsequent ideas on the subject. It offers a satisfactory explanation for many cases of urticaria in which sensitiveness may be transferred by the injection of serum from a sensitive subject to a normal subject, but is not altogether satisfactory for the explanation of many forms of bacterial sensitization and contact dermatitis. These variations, dependent on the animal used, the method of application and the substance under test, are cited merely to show that laboratory and clinical experiments must be studied with great care and repeated with many variations of detail before valid generalizations can be drawn.

Bacterial proteins [4] may be used in the demonstration of anaphylaxis, and the sensitization may be passively transferred, the passively sensitized animal reacting to a dose of the specific bacterial protein by a general anaphylactic reaction, but such animals rarely show a local reaction when the test substance is applied to the skin. The two reactions—general anaphylaxis and the delayed cutaneous reaction typified by the tuberculin test—are apparently due to different mechanisms. For the production of the type of cutaneous sensitization revealed by the tuberculin test, the existence of an active inflammatory process, past or present, appears to be essential, and this sensitization cannot be passively transferred.

These three types of reaction—foreign serum anaphylaxis, bacterial anaphylaxis and the delayed cutaneous reaction to bacterial products—occur in nearly all individuals of a species in the manner characteristic for that species. The reaction may be considered normal, in that every individual of the species responds in about the same way.

DISTINCTION BETWEEN ALLERGY AND IMMUNITY

Allergy developing in parasitic disease is also a fairly constant specific quality, though there is no explanation of why it should be stronger in some subjects than in others. At the outset it must be understood that allergy and immunity are totally distinct processes and do not necessarily run parallel to each other. Although in some cases an allergic reaction may be an aid to immunity, allergy may exist without immunity

4. Kraus and Doerr: Bacterial Anaphylaxis, Wien. klin. Wchnschr. **21**:1008, 1908. Baldwin: Studies in Immunity to Tuberculin, J. M. Research **22**:189, 1910.

and immunity without allergy, as shown by Rich [5] in a series of enlightening experiments. The first experiments concerned acquired immunity without allergy. Rabbits were infected with syphilis by various routes, and lesions developed in all. When inoculated a second time, from one hundred and eighty-eight to three hundred and forty-four days later, no symptoms developed. The animals were immune, but showed no allergic reaction. The second experiments deal with passive transfer of immunity, without sensitiveness. Animals were rendered immune to pneumococcus by vaccination, and their serum was then introduced intravenously into normal animals which were then infected with virulent organisms. The latter animals survived millions of doses of virulent bacilli and were relatively indifferent to the presence of the pneumococcus, while actively immunized animals reacted with exaggerated local damage and inflammation. In the third experiments the hypersensitiveness of the immune allergic animal was removed by desensitization, and the immunity left intact. Rabbits were rendered immune and allergic to the pneumococcus and to the bacillus of fowl cholera by vaccination with dead organisms, and half of each series were then desensitized by the intravenous injection of relatively large amounts of killed vaccine. The immune desensitized animals, the immune undesensitized animals and normal controls were then given intracutaneous injections of virulent living organisms. The immune desensitized animals showed the minimal reaction to infection; the immune undesensitized animals survived, but far larger destructive lesions developed, while in the normal controls large destructive lesions developed and death occurred. In immunized animals in which allergy was excluded, the tissues were remarkably indifferent to the infecting bacteria which were undergoing destruction, as in natural immunity; there was no appreciable death of tissue, inflammation was negligible and immobilization of bacteria was just as effective as in allergic reaction.

SYPHILIS

In discussing allergy due to parasites, it may be well to begin by describing some of the observed facts which are believed to be due to allergy, as they occur in three diseases: syphilis, tuberculosis and tinea. The chancre is apparently the reaction of normal tissue to the spirochete. Its appearance is followed by a period during which there are no other symptoms, but during which the organisms are scattered through the body, and the reaction of the blood serum is changed, as shown by the development of a positive Wassermann reaction. At the end of this period an eruption appears, and this eruption does not consist of mul-

5. Rich: Bacterial Allergy and Acquired Immunity, Tr. Nat. Tuberc. A., 1931, p. 149.

tiple chancres, but is erythematous or papular. It is caused by the germ or by its toxins, or both, but its appearance is absolutely different from that caused by local inoculation in a healthy subject, no matter how that inoculation may have been performed. We assume, therefore, that the skin has become allergic to this particular virus. Organisms are present in the lesions of the skin and mucous membrane, often in enormous numbers, but this does not prove that the skin is not allergic; it only proves that the tissue has not yet acquired in full strength the power of destroying the offending organisms. The lesion is properly called a syphilid, an eruption caused by the action of a pathogenic organism on a sensitized skin.

Later in the disease the cutaneous lesion has an entirely different character. It is permanent instead of transient and large and infiltrated instead of small and superficial, and leaves scars on healing. In other words, the reaction of the skin has changed; the type of allergy is different, more inflammatory. These late lesions of the skin contain few spirochetes, the skin has become sensitive to the presence of small numbers of organisms and responds by a reaction which contrasts strongly with the mild reaction of the secondary stage, and at the same time it has acquired the power of inhibiting, to a certain extent, the growth of the organisms. In tertiary syphilis, therefore, allergy, i. e., the increased sensitivity of the skin, and partial immunity, shown by destruction of the parasite, run courses which are roughly parallel. In malignant syphilis, however, allergy, i. e., the exaggerated response, with the destruction of tissue, is even greater, but immunity can hardly be said to exist, as many of these patients die of the infection.

TUBERCULOSIS

The tuberculids, at first thought to be due to the toxins of tuberculosis, are now known to be caused in many cases, if not in all, by the bacillus itself. The factor which determines whether a given lesion will develop into a tuberculid or an active form of tuberculosis, like scrofuloderma or tuberculosis verrucosa, is not the presence or absence of the bacillus, for this may be present in either, but the reaction of the skin itself, and this reaction is of two kinds—the inflammatory response of the tissue, and the killing of the bacillus. In scrofuloderma, the inflammatory reaction is great and the lethal action on the bacillus comparatively slight; in tuberculosis verrucosa, the inflammation is less and the lethal action somewhat greater, while in the tuberculids, as a rule, the inflammation is comparatively slight, while the invading parasites are soon killed and the lesion heals without treatment. In these conditions, allergy varies inversely with immunity. Nevertheless, in erythema

induratum the inflammatory reaction is great, and so also is the lethal action of the tissue on the parasite. In this instance, allergy varies directly with immunity. The two reactions, allergy and immunity, bear no necessary relation to each other. If any of the sarcoids are to be considered tuberculous, as is probable, there is a tuberculid which introduces yet another variation; for the development of sarcoid is an allergic reaction, and yet patients with sarcoid show a lower percentage of susceptibility to the tuberculin test than do the average members of the adult population.[6]

TINEA

Trichophytid is in many ways analogous to tuberculid, but opens up a whole new vista for exploration. Transient trichophytids are now generally recognized. They may be erythematous, lichenoid, vesicular or nodose, or resemble pityriasis rosea or erythema multiforme. Mycelia have been found in many of these lesions, in their very early stages, but not, so far as I am aware, after the first few days. As in tuberculid, the determining factor in the lesion is not the presence or absence of the parasite, but the altered reaction of the skin. Vesicles occur both in the primary focus and in trichophytid, but whereas in the former they are usually fairly deep, with thick roofs, in the latter they are usually more superficial and thin-roofed, with little surrounding inflammation. The other transitory trichophytids, the ordinary lichenoid or the rarer erythematous and nodose types, do not resemble any primary focus of tinea and suggest immediately a toxic eruption. The chronic trichophytids are in a different group and are still debatable. The diagnosis is badly overworked, and many eruptions so classed are undoubtedly dermatitis of external origin. But there remains a large group of lesions which so closely resemble tinea, that one is almost forced to believe that they are a manifestation of tinea. The only thing that stands in the way of this diagnosis is the absence of the parasite. If tinea organisms are found, the eruption is tinea. But how can one explain the lesions that look like tinea, but yield no parasite? The answer is, I think, easy if one remembers that there are two elements in every infection—the altered reaction of the tissue, which is allergy, and the power of the tissue to destroy the parasite, which is immunity—and that these two elements may vary independently of each other. Confining ourselves for the moment to cases of infection of the foot, in the most mild type there is little allergy and no immunity; symptoms are slight and mycelia are found readily. In some severe cases, allergy is certainly present, as shown by severe spreading inflammation, and

6. Sulzberger and Wise: Tuberculin, Report to the Dermatological Staff of the New York Post-Graduate Medical School and Hospital, Jan. 8, 1931.

yet the parasites are easily found; there is little immunity. In some severe chronic cases, allergy is present, as shown by severe and extensive inflammation, and immunity has developed; it may even be impossible to find a parasite, although it was present in the early stages. The chronic cases of infection of the hands may be explained as a local infection, usually secondary to a focus elsewhere and usually blood-borne in a skin which has become allergic, with an immunity in some cases great enough to kill all organisms brought to it, but which is reinfected from time to time from the primary focus; in other cases, the skin does not have enough immunity to kill all organisms brought to it, but always harbors a few in the deeper layer—so few that they are not found—and probably these have insufficient vitality to be cultivated. The trichophytids illustrate another important feature of allergic response—the tendency to select a certain tissue, like the skin, and even certain parts of that tissue to the exclusion of others. Trichophytid accompanying kerion of the scalp or beard is usually lichenoid, and occurs on the neck or trunk. The eruption is seldom vesicular, and the hands are rarely, if ever, involved. Trichophytid complicating tinea pedis, however, is usually vesicular, and usually involves the hands or feet; the rest of the surface is seldom affected. I have no explanation for this observed fact.

The trichophytin reaction is still under discussion, and is not yet standardized. Intracuticular injections of dilute solutions seem to be the most satisfactory, giving few or no false positive reactions and very few negative reactions in clinically positive cases. A positive reaction in a clinically negative case is generally explained as a persistent reaction, left by a long extinct or an asymptomatic infection, and this is possible. Amberg [7] reported a case of deep tinea in which a positive trichophytin reaction was obtained twenty-nine years later. It is possible that in some cases the reaction is not specific. Patients with Monilia infection are reported to give a positive reaction to trichophytin. The test should be controlled by an injection of the culture medium.

The value of injection of trichophytin as a means of treatment is still to be proved. It must be considered, I think, as a means of desensitization, and as such must be handled with care, the dose being large enough to produce a mild local reaction, but not large enough to cause a general reaction and increase of sensitization. I see no reason to believe that it can have any effect on the infection itself.

Allergy to Monilia infection has been reported, with eruptions described as moniliid, and cutaneous sensitization to moniliin, but the subject needs much further study.

---

7. Amberg: J. Exper. Med. **12**:435, 1910.

BACTERIAL SENSITIZATION

Bacterial sensitization in other branches of medicine is well recognized, a large part of the reaction to infection being allergic. There are two types which interest the dermatologist particularly—the localized, sharply defined and the generalized or eczematous lesions. Urticaria, which may have many causes, but which is usually ascribed to specific food sensitization, is more often due to an infection. Acute or chronic [8] erythema multiforme, as a complication of acute articular rheumatism, is also a definite allergic manifestation of bacterial sensitization, as are also some cases of erythema nodosum and of erythema induratum. Cases of urticaria following digestive disturbances are probably also of bacterial origin, the action of the parasite taking place within the intestinal canal instead of in the tissues. In all cases of that sort, therefore, ranging from urticaria to purpura, a focal infection should be sought as a possible source of the toxin responsible for the eruption. The generalized or eczematous type is less commonly recognized as caused by focal infection, but reports are accumulating of cases of eczema which had resisted the most varied treatment and in which recovery followed the removal of such a focus.[9] Food allergy has received a great deal of careful study, but does not loom so large as it did a few years ago. It is certainly one of the causes of urticaria, at all ages, and of eczema in infancy. Its importance as a cause of eczema in adult life is slight. The very mention of it brings up the question of cutaneous tests, and cutaneous tests of food substances have been very disappointing, as a patient will often react to many substances, only one of which can be shown to bear any relation to the eruption, and susceptibility to the test may be found to vary from time to time, without apparent cause. Sensitization may be transferred by the injection of serum from a susceptible patient (a procedure very valuable in diagnosis), and desensitization may be accomplished by gradually increasing doses. The surest method, both for diagnosis and for treatment, is to determine the offending food by elimination from or addition to the diet, and then to avoid it.

CONTACT DERMATITIS

Contact dermatitis is the most confusing of all the groups. Some irritants, the caustics, produce the same effects on all skins, and for the purpose of this discussion may be disregarded. Others, like poison ivy and primrose, affect ordinarily a considerable fraction of the popu-

8. Rackenmann, F. M.: Clinical Allergy, Particularly Asthma and Hay Fever, Mechanism and Treatment, New York, The Macmillan Company, 1931, p. 233.

9. Rackemann,[8] p. 55.

lation, and even those apparently immune may be affected if the dose is sufficiently concentrated and repeated. It is generally believed that that is a true sensitization phenomenon and that the first exposure is not followed by any ill effect, but this has not been proved, although it seems to be established that repeated exposure increases the sensitiveness. Other substances, like some of the pollens, affect only a small proportion of the population. Coca [10] and his followers claim that this kind of sensitiveness has nothing to do with atopy, the hereditary quality by virtue of which certain people become sensitized to certain substances which produce hay fever and asthma. He was able to separate two substances from ragweed pollen, one of which, oil-free, produced a strong reaction on a mildly sensitive patient with ragweed hay fever, but no reaction to the patch test on a patient with eczema, and the other, atopen-free, which produced no reaction on a very sensitive patient with ragweed hay fever, but a strong reaction to the patch test on a patient with eczema. When patch tests with this dermatitis-producing substance were made on forty persons with ragweed hay fever, forty subject to other diseases and forty without individual or family atopic history, a positive reaction was obtained in six of each group, showing, Coca stated, that sensitiveness of the skin is independent of the hereditary sensitiveness of hay fever. His separation of two substances having different actions is convincing and in line with results of other observers, but his conclusion as to the independence of the two types of sensitiveness is not borne out by the clinical experience of most observers, who find a very high incidence of hay fever and other definitely allergic diseases in the personal and family history of their patients with chronic eczema. The majority of cases of chronic eczema belong in this group; the possible causes are innumerable, and the etiologic diagnosis is correspondingly difficult. The best method of approach is to take the history carefully and supplement this by patch tests with the suspected substance. Intracutaneous and scratch tests are not so valuable in this connection. Once the offending substance is discovered, the best treatment is to avoid it, though desensitization may be attempted. It must be remembered that a patient may be exposed to the irritant for months or years before sensitization is effected, so the attempt to incriminate a substance which first touched the skin a short time before the outbreak is often futile. Also the same subject may be sensitized to a large number of irritants, all of which must be eliminated if the eruption is to be cured. It must be remembered also that sensitization may be local—the parts of the skin which have been most exposed become the most irritable—while the rest of the surface may retain its native immunity.

---

10. Brown, A.; Milford, E. L., and Coca, A. F.: Studies in Contact Dermatitis: Nature and Etiology of Pollen Dermatitis, Allergy **2**:301 (July) 1931.

These cases of contact dermatitis caused by a substance quite innocuous to the vast majority of people seem at first sight to be in a different class, displaying a true idiosyncrasy, but there are all grades from the most exceptional excitants to the commonest, and the difference is often only apparent and dependent on opportunity for repeated exposure. Nevertheless, there are constitutional differences; some persons are more easily sensitized than others, and this capacity for sensitization is a hereditary quality. Heredity is evident in hay fever and asthma; it is still in dispute in contact dermatitis, but careful investigation brings to light a surprisingly high percentage of other allergic symptoms in cases of chronic eczema. Why one tissue rather than another should become sensitized is still a mystery.

ABSTRACT OF DISCUSSION

Dr. Samuel Ayres, Jr., Los Angeles: I think that the work Dr. Williams has done emphasizes something of which most of us do not take sufficient cognizance, that is, allergy and immunity. My feeling is that in these cases of phytids one is dealing with partial immunity plus allergy. Immunity has developed in the blood stream but not in the skin. In cases of smallpox or scarlet fever, after the person recovers the epithelial tissues are immune but not allergic. Superficial contact with the organism does not produce an allergic reaction. In fungous infection there is not such cutaneous immunity. The fungus can continue to grow on the skin, but when it gains entrance to the blood stream the organism is destroyed, presumably by circulating immune antibodies. The phytids are supposed to be caused by the effects of the killed fungi or their products on the epidermis which has become sensitized. The fact that epidermal immunity develops in the fungous infections of the scalp in adults would lead one to think that investigations along that line might be profitable.

LXVI.—LIPIDS OF THE SKIN

INFLUENCE OF SOME FACTORS ON THE ALBINO RAT

D. J. KOOYMAN, PH.D.

ST. LOUIS

In a recent review of the subject of skin lipids[1] it was pointed out that most tissues of the animal body have been found to maintain a remarkably constant level of certain lipids, particularly cholesterol and phospholipids, in spite of extreme changes in the nutritional status of the animal. This fact suggests that the life and normal function of the cells of a tissue require a definite level of these lipids.

Recent reports in the literature indicate that the skin may be an exceptional tissue since it has apparently been demonstrated that the cholesterol content at least can vary between rather wide limits. Buschke and Markus [2] have reported that cholesterol-containing lipids were greatly diminished or entirely absent in the skins of rats with alopecia produced by thallium acetate. Roffo has found a marked increase in the cholesterol of the skin of rats exposed to sunlight or ultraviolet rays [3] and a diminution in the cholesterol of the skins of rats kept in the dark.[4] Kawaguchi [5] also found that solar or ultraviolet irradiation increased the cholesterol content in the skins of guinea-pigs and rabbits.

Since phospholipids as well as cholesterol apparently play an important rôle in the physiology of the cell, and as no fundamental study has been made of the phospholipid content of the skin, it was proposed to study simultaneously the cholesterol and phospholipid content of the skin of normal rats and those treated with the agents which were found to produce such remarkable changes in the cholesterol content.

Studies, observations and reports from the Barnard Free Skin and Cancer Hospital and the School of Medicine, Washington University, Department of Dermatology and Medicine, service of Drs. M. F. Engman and W. H. Mook, St. Louis, Mo.

1. Kooyman, D. J.: Lipids of the Skin, Arch. Dermat. & Syph. **25**:245 (Feb.) 1932.

2. Buschke, A., and Markus, A.: Untersuchungen über die Beziehungen des Thalliums zum Lipoidstoffwechsel und zum Gewebe, Klin. Wchnschr. **8**:1122, 1929.

3. Roffo, A. H.: Apropos de la propriété héliotropique de la cholestérine en rapport avec le cancer de la peau, J. de physiol. et de path. gén. **28**:854, 1931.

4. Roffo, A. H.: La photoactivité de la lumière sur la cholesterine de la peau, J. de physiol. et de path. gén. **29**:739, 1931.

5. Kawaguchi, S.: Ueber den Einfluss der Lichtstrahlen auf den Gesamtcholesteringehalt der Haut, Biochem. Ztschr. **221**:232, 1930.

Burr and Burr [6] and others [7] have observed a peculiar condition of the skin in rats fed on a diet deficient in fat. It was also thought interesting to study the cholesterol and phospholipid content of the skins of rats kept on a fat-deficient diet.

One group of rats was treated with thallium acetate; another group received ultraviolet irradiation; a third group was fed a fat-deficient diet, and a fourth group, untreated, was kept as a control.

In the light of earlier work, the results of analyses show surprisingly little difference in the cholesterol as well as in the phospholipid content of the skins of the rats in the four groups, in spite of the different treatment they received. The results will be discussed.

EXPERIMENTAL DATA

The skin is perhaps one of the most difficult tissues from which to obtain a standard or uniform sample. Some considerations which make it difficult are: 1. The composition of the skin may vary with the region of the body from which it is removed. 2. The water content of the skin is variable. 3. It is practically impossible to remove all of the subcutaneous tissue with its variable fat content from the sample by dissection.

The first of these difficulties was obviated by using the entire pelt of the animal with the exception of the head and tail. The second and third were overcome by preparing the samples as uniformly as possible and basing the analyses on the water-free, lipid-free weight of the extracted sample.

The skin was prepared and extracted as follows: The rat was weighed, stunned by a blow on the head, and the skin, except that on the head and tail, removed. The adhering subcutaneous tissue and fat were removed as completely as possible, and the skin was fastened with thumb tacks to a smooth, clean board. The hair was removed by clipping closely with a fine clipper and shaving with a dry razor. The skin was then cut in long narrow strips and weighed (moist weight). The strips were cut in tiny bits into a flask containing 50 cc. of a 95 per cent solution of alcohol. The alcohol was heated to the boiling point and when cool was poured into a filter paper extraction thimble. The alcoholic extract which filtered through the thimble was saved and combined with later extracts. The thimble and the skin were placed in an all glass extraction apparatus and extracted with hot alcohol vapors for twenty hours. The alcoholic extract was replaced with fresh alcohol after three and six hours of extraction. The combined alcoholic extracts were evaporated under diminished pressure, and the residue was taken up in ethyl ether. This ether extract was filtered and made up to volume in a 100 cc. volumetric flask. Aliquot parts of this extract were used for the various analyses. The extracted sample of skin was carefully dried and weighed (extracted weight).

The completeness of extraction by this method was tested by hydrolyzing several samples of extracted skin with a 50 per cent solution of sodium hydroxide, extracting the acidified reaction mixture with ethyl ether, evaporating the ether

6. Burr, G. O., and Burr, M. M.: A New Deficiency Disease Produced by the Rigid Exclusion of Fats from the Diet, J. Biol. Chem. **82**:352, 1929.

7. Sinclair, R. G.: Some Observations on the Growth of Rats on a Fat-Free Diet, Proc. Soc. Exper. Biol. & Med. **27**:1059, 1930. Graham, C. E., and Griffith, W. H.: Observations on the Nutritive Value of Certain Fats, ibid. **28**:756, 1930.

extract to dryness and weighing the material which could be extracted from the residue with petroleum ether. In spite of the long period of extraction, the samples were found to contain from 1 to 1.5 per cent of lipids. The total lipids already extracted, however, amounted to about 50 per cent of the extracted weight, so that the extraction was 97 per cent complete.

Total lipids were estimated by transferring an aliquot part (usually 5 cc.) of the ether extract to a weighed flask, evaporating the ether and drying to constant weight. In cases in which the total lipids were low, Bloor's [8] oxidation method was used.

Cholesterol and cholesterol esters were estimated by a modified Okey digitonin method.[9] Phospholipids were estimated indirectly from the lipid phosphorus value found by the Whitehorn method.[10]

OBSERVATIONS

Effect of Size on Skin Lipids.—Although rats of approximately the same size and age were used in these experiments, they did not all grow at the same rate. Those receiving ultraviolet irradiation had the most rapid, and those on a low fat diet the poorest, rate of growth. Consequently at the time of analysis there was considerable difference in the average weight of the rats in the four groups. There were also differences in the rates of growth of rats in the same group.

When skins of animals of a group were analyzed it was found with striking regularity that those of the large rats had the lowest, and those of the small rats, the highest, lipid content. It seemed only logical, therefore, that comparisons should be made between the lipid contents of the skins of rats of the same size. In order to do this, the skins of control animals of various sizes were analyzed. When the cholesterol and phospholipid contents of these were plotted against body weight, the points fell as shown in figure 1. Body weight is influenced by variables such as fat and water content, and it is possible that these are responsible for much of the dispersion of the points. Less scattering would perhaps have been found if the lipid values had been plotted against a more constant criterion of size such as body surface area. It is regrettable that the length measurement necessary for the calculation of surface area was not made. Nevertheless, a smooth curve can be drawn through the mean positions of the points as plotted in figure 1.

Although the absolute amount of cholesterol and phospholipid in the skin increases steadily with increasing size, the relative or percentage

8. Bloor, W. R.: The Determination of Small Amounts of Lipid in Blood Plasma, J. Biol. Chem. **77**:53, 1928.

9. Okey, Ruth: A Micro Method for the Estimation of Cholesterol by Oxidation of the Digitonide, J. Biol. Chem. **88**:376, 1930.

10. Whitehorn, J. C.: A Method for the Determination of Lipoid Phosphorus in Blood and Plasma, J. Biol. Chem. **62**:136, 1924.

amount diminishes. The curves for extracted skin show a definite downward trend which is rapid at first and becomes more gradual with increasing weight. For moist skin the curves are much flatter, rise slowly at first, pass through a maximum point and slope slowly downward. The curves for moist skin are actually the result of the addition of the curve for lipid content and the curve for water content of the skin. The loss of water from the skins of young rats is more rapid than the diminution in lipids, causing an apparent increase in the lipid content of

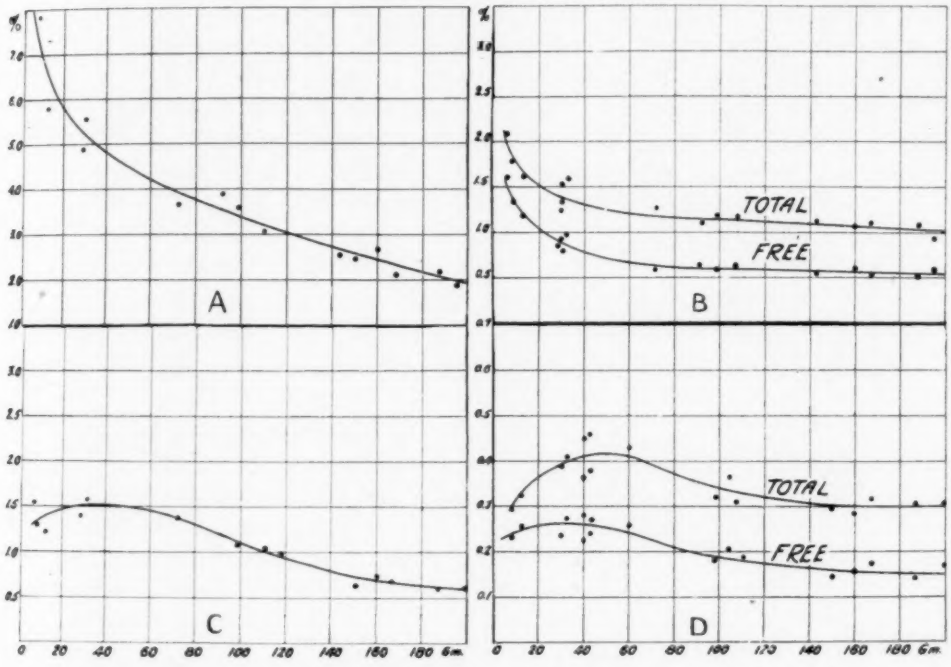


Fig. 1.—Charts in which the lipid content of the skin in per cent is plotted against body weight for control rats: *A*, phospholipid in extracted skin; *B*, cholesterol in extracted skin; *C*, phospholipid in moist skin; *D*, cholesterol in moist skin.

the moist skin. It is interesting to note that these curves are of the same general form as those found by Sinclair [11] for the total unsaponifiable and phospholipid fatty acid content of the whole rat, and that he found the lipid content of a runt to be more like that of a normal rat of the same size than that of one of the same age.

11. Sinclair, R. G.: The Metabolism of Phospholipids: II. The Influence of Growth on the Phospholipid and Cholesterol Content of the White Rat, J. Biol. Chem. **88**:575, 1930.

Bürger and Schlomka,[12] Meyer[13] and Hentschel[14] have also found that the total sterol content of human skin decreases with age. Bürger has suggested that this is due to an atrophy or disappearance in the skin of glandular elements rich in cholesterol. The fact that the diminution is continuous throughout life suggests a slower development of the glandular elements of the skin rather than a degeneration. The epidermis and its glands with a high phospholipid and cholesterol content develop slower than do the other structures of the skin, so that as the animal becomes larger, the skin contains a higher percentage of elastic and connective tissue which have a relatively low phospholipid and cholesterol content.

The ratio of free to total cholesterol is higher in the skins of small rats, but it soon reaches a rather constant value. This can be explained by a lower percentage of keratinized tissue, containing combined cholesterol, in the skin of young rats. The ratio of phospholipid to cholesterol also decreases with increasing size, as is apparent from the difference in slope of the two curves. According to the findings of Milbradt,[15] all of the cholesterol in the skin is not an integral part of protoplasm, but some at least is present as stored sterol. Since just how much of the cholesterol in the skins analyzed was stored and how much was essential is not known, the ratio of phospholipid to cholesterol has no great significance in the interpretation of the data.

Effect of Thallium Administration on Skin Lipids.—Young rats, weighing approximately 60 Gm., were given 0.02 mg. of thallium acetate daily, by mouth. In from ten to fourteen days they began to show toxic symptoms, such as diarrhea, loss in weight, paralysis and a loss of hair. The drug was discontinued and in from three to five days the skins were removed and analyzed as has been described. None of the animals became totally bald, but all had large denuded areas along the back extending from the head to the rump.

The lipid values for the skins of rats treated with thallium acetate are shown as small rectangular points on the charts of figure 2. The curves of figure 2 are those for control rats. The points for the phospholipid content all lie above the curve for extracted skin and are

12. Bürger, M., and Schlomka, G.: Beiträge zur physiologischen Chemie des Alters der Gewebe: IV. Untersuchungen an der menschlichen Haut, Ztschr. f. d. ges. exper. Med. **63**:105, 1928.

13. Meyer, Alice: Vergleichende Gesamtsterin- und Sterinesterbestimmungen der Haut des wachsenden und erwachsenen Organismus, Ztschr. f. Kinderh. **50**: 586, 1931.

14. Hentschel, H.: Ueber den Gesamtsterin und Ergosterinaushalt während der Entwicklung des Organismus, Ztschr. f. Kinderh. **52**:623, 1932.

15. Milbradt, W.: Lipämiestudien, Biochem. Ztschr. **223**:278, 1931.

evenly distributed above and below the curve for moist skin. There is, therefore, a significant increase in the phospholipid and water content of the skin. The cholesterol values indicate an increase in free, but no change in total, cholesterol content, or a decrease in combined cholesterol.

These results are not in agreement with the histochemical results obtained by Buschke and Markus.[2] They are, however, in accord with the histologic changes produced in the skin by the administration of thallium acetate. According to Dudits [16] there is enlargement of the

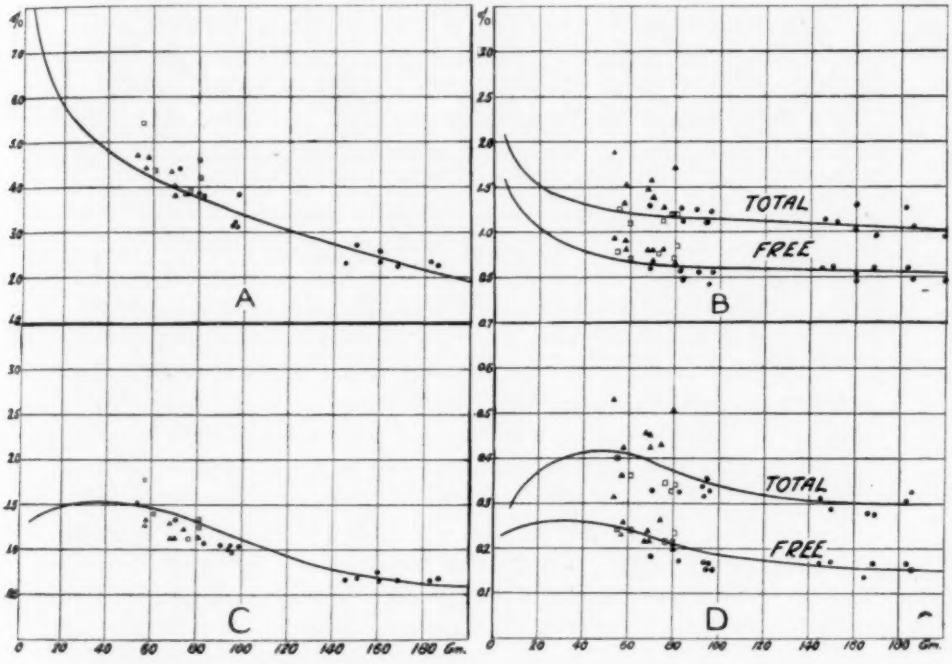


Fig. 2.—Charts in which values for the lipid content of the skins of treated rats are plotted against body weight. The curves are those found for control animals. The square indicates rats treated with thallium acetate; the circle, rats treated with ultraviolet irradiation; the triangle, rats given a diet low in fat. *A*, phospholipid in extracted skin; *B*, cholesterol in extracted skin; *C*, phospholipid in moist skin; *D*, cholesterol in moist skin.

follicles, irregular keratinization and a shedding of hair. An enlargement of follicles would be accompanied by an increase in phospholipids and free cholesterol, and irregular keratinization by a decrease in cholesterol esters, a characteristic product of keratinization. Irritated or inflamed skin would also be expected to have an increased water content.

16. Dudits, A.: Thallium Poisoning, Magyar orvosi arch. **32**:249, 1931; abstr., Chem. Abstr. **25**:4626, 1931.

Since Bloor [17] has found that phospholipid content roughly parallels physiologic activity, the enlarged follicles and high phospholipid content would explain the rapid regrowth of hair when the drug is withheld and the stimulating effect of small doses of thallium acetate on hair growth observed by Cooper and Engman.[18]

Effect of Ultraviolet Irradiation on Skin Lipids.—Six rats were exposed to irradiations from a Uviarc lamp for thirty minutes at a distance of 30 inches six days a week for three weeks before the skins were analyzed. This dosage was continued in spite of the fact that the first exposures caused some necrosis at the margin of the ears.

The lipid values for these rats are shown as circular dots for animals weighing from 70 to 100 Gm. in figure 2. The mean position of the points for the phospholipid content of extracted skin lies very near the curve for control rats. Irradiation has, therefore, produced no significant change in the phospholipid content of the skin. There is also but little change in the cholesterol content, the mean value for total cholesterol content being only a little above the curve for control rats. The points for free cholesterol, however, all lie below the curve and indicate a slight decrease in free cholesterol. Since the total cholesterol content is increased and the free cholesterol content decreased, irradiation has evidently caused an increase in the combined cholesterol of the skin. The irradiated skin has an increased water content, and consequently the lipid values calculated for moist skin lie below the curves for control skins.

The hair of the animals obviously prevents a large part of the radiation from reaching the skin. That which does reach the skin of the irradiated animals is certainly greater than that which reaches the skin of the controls and should produce effects at least as great as those due to the difference in radiation reaching the skin of rats kept in the dark and rats kept in a naturally lighted room, reported by Roffo.[4]

In order to rule out the shielding effect of hair, a number of rats were epilated with barium sulphide and allowed to recover from the irritation for three days. Half of the group were kept as controls, and the others were given a single exposure of thirty minutes at 30 inches to irradiation from a Uviarc lamp. After from five to seven hours an erythema had developed, and the skins were removed and analyzed. The rats in this group were larger, and the lipid values for the skins are shown as circular dots in figure 2 for rats weighing 140 to 200 Gm.

17. Bloor, W. R.: Distribution of Unsaturated Fatty Acids in Tissues: III. Vital Organs of Beef, J. Biol. Chem. **80**:443, 1928.

18. Cooper, Z. K., and Engman, M. F.: A Study of the Stimulating Effect of Small Doses of Thallium Acetate on the Rate of Growth of Hair in the Albino Rat, Arch. Dermat. & Syph. **23**:1031 (June) 1931.

Here again the distribution of points is very much the same as for the values of the skin lipids of control animals. No significant change has been produced in the phospholipid or free cholesterol content and only a slight increase in the total cholesterol content.

The Effect of a Diet Low in Fat on Skin Lipids.—Young rats weighing approximately 30 Gm. were kept in cages provided with false bottoms of coarse screen and given a diet consisting of sucrose 80 per cent, extracted casein 16 per cent, salt mixture (McCollum's 185) 4 per cent, and daily doses of 3 drops of cod liver oil and 0.5 Gm. of ether-extracted yeast.

The skins were analyzed after a period of five weeks on this diet. This time was not sufficient for the classic signs of the vitamin F deficiency disease, namely, necrosis of the tail and scaliness of the legs, skin and tail, to develop, but was sufficiently long to produce some of the early signs such as abnormal growth, diarrhea and excessive dandruff on the back. This period should also have been sufficiently long to produce a change in the lipids of the skin if they are influenced by the amount of fat in the diet.

The lipid values for the skins of the rats in this group are plotted as triangular points in the charts of figure 2. These show a slight but hardly significant increase in phospholipids and an increased total cholesterol, free cholesterol and water content. Contrary to expectation, the lipids increased rather than diminished on a low fat diet, and it is interesting that the skins of these animals had grossly a much more oily appearance than those of animals of the other groups.

COMMENT

In these experiments the entire skin has been considered as a single homogeneous organ, which, of course, it is not. Since the epidermis constitutes such a small proportion of the whole skin, marked changes in its composition would produce but slight, if any, perceptible changes in the composition of the skin as a whole. Analyses of the epidermis alone would, no doubt, reveal interesting changes in the skins of animals treated with thallium acetate, which acts primarily on the hair follicles and glandular elements of the epidermis, and in those of animals treated with ultraviolet radiation since the effects due to the absorption of the light are necessarily produced in the epidermis.

Of the factors studied, the size or development of the skin was found to have the greatest influence on its phospholipid and cholesterol content. This may be due in part to the fact that the epidermis with a high content of these lipids tends to maintain a constant thickness, while the corium with a lower content of these lipids becomes increasingly thicker.

It is interesting that such radically different treatment as the rats in these experiments received should so little affect the cholesterol and phospholipid content. These results demonstrate the constancy of a normal level of these lipids in a tissue and confirm in general the conclusions of Mayer and Shaeffer [19] concerning the nonvariable nature of these lipids.

SUMMARY

The cholesterol and phospholipid content of the skin of the white rat was found to diminish with increasing size. By plotting the lipid contents of the skins of normal rats of various sizes against body weight, curves were constructed. When the lipid contents of the skins of animals epilated with thallium acetate, exposed to ultraviolet radiation, or kept for a time on a low fat diet were plotted on these same charts, the points fell surprisingly near the normal curve, although the following trends were observed:

	Phospholipid Content	Free Cholesterol Content	Total Cholesterol Content
Rats treated with thallium acetate.....	Increased	Increased	Unchanged
Rats irradiated with ultraviolet rays....	Unchanged	Decreased	Unchanged
Rats on low fat diet.....	Increased	Increased	Increased

19. Mayer, A., and Shaeffer, G.: Recherches sur la teneur des tissus en lipoïdes, J. de physiol. et de path. gén. **15**:773, 1913.

THE QUESTION OF BISMUTH PENETRATION OF THE NERVOUS SYSTEM

REPORT OF CLINICAL AND LABORATORY STUDY

JOSEPH V. KLAUDER, M.D.
AND
HERMAN BROWN, B.S.
PHILADELPHIA

Reported studies of the penetration of bismuth into the nervous system have been conflicting. The results of studies of the penetrability of nerve tissue for bismuth by a number of investigators have been reviewed in recent reports by Hanzlik and his collaborators [1] and need not therefore be detailed. Bismuth has rarely been found in the spinal fluid of patients into whom a bismuth compound has been injected, and only occasional traces have been found in the brains of laboratory animals into which massive doses of bismuth compounds have been injected. Hanzlik and his collaborators,[2] however, employing a new bismuth compound, sodium iodobismuthite (iodobismitol), which is later discussed, have reported a high degree of penetrability of the nervous system for this compound. On the other hand, Levaditi, Vaisman, Manin and Schoen [3] were unable to find bismuth in the spinal fluid of patients into whom sodium iodobismuthite was injected. Traces of bismuth were found in the brains of laboratory animals in which sodium iodobismuthite was injected in the same frequency as in the series of animals into which carboxethylmethyl nonoate basic bismuth was injected.

We report herewith our studies to determine the presence of bismuth in the spinal fluid of patients treated with different compounds of bismuth and in the brains of rabbits likewise given injections of different compounds of bismuth. In other patients treated with bismuth com-

---

Contribution from the Research Institute of Cutaneous Medicine and the Clinic for the Treatment of Ocular Syphilis, Wills Hospital.

1. Hanzlik, P. J., and Spaulding, J. B.: Cerebral Penetration of Bismuth: Experimental Results with Iodobismuthite, Iodobismitol and Some Other Bismuth Products, Am. J. Syph. **16**:335, 1932.

2. Hanzlik, P. J.; Mehrtens, H. G., and Spaulding, J. B.: Cerebral and Spinal Fluid Penetration of Bismuth: Clinical Results with Iodobismuthite (Iodobismitol) and Some Other Bismuth Products, Am. J. Syph. **16**:350, 1932.

3. Levaditi, C.; Vaisman, A.; Manin, Y., and Schoen, R.: Diffusion of Bismuth into the Brain and Its Penetration into the Spinal Fluid, Bull. Soc. franç. de dermat. et syph. **40**:738 (May) 1933.

pounds, the spinal fluid was examined after fever therapy and also after subdural injections of serum as employed in the Swift-Ellis method of treating neurosyphilis in order to determine if these therapeutic measures affected the penetration of the nervous system by bismuth. It is to be recalled that vasodilatation which occurs in the state of fever and a sterile meningitis which is produced in the Swift-Ellis therapy have been claimed to facilitate the passage of drugs from the blood into the nervous system.

CLINICAL STUDY

The spinal fluid of two groups of patients was examined for bismuth. The first group comprised eighteen patients with neurosyphilis, the majority of whom had optic atrophy. Each patient was treated with a bismuth compound. The following preparations were employed: bismuth hydroxide suspended in oil, bismuth salicylate suspended in oil, sodium and potassium bismuth tartrate suspended in oil and a lipoid soluble bismuth compound, bismuth camphocarboxylate (bismocymol).

The amount administered prior to examination of the spinal fluid varied from six injections of 0.1 Gm. of the metal bismuth, administered at weekly intervals, to fifty injections of 0.1 Gm. In a few patients the blood and urine were examined for bismuth at the same time the spinal fluid was examined. Bismuth was found in the blood and urine of all specimens examined. In three patients, the spinal fluid was examined after fever produced by diathermy, and in two patients, after fever produced by malaria. The spinal fluids of these patients were withdrawn just at the end of this fever therapy. A bismuth compound was injected during the course of the fever. In four patients the spinal fluid was examined after the Swift-Ellis treatment. In each of these four patients there was a different interval between the subdural injection of serum as part of the Swift-Ellis treatment and the withdrawal of spinal fluid for examination for bismuth. The intervals were as follows: fifteen minutes, thirty minutes, ten days and two weeks. Spinal fluid was withdrawn by lumbar puncture in some patients and by cisternal puncture in others. The amount of spinal fluid examined for bismuth varied from 5 to 32 cc. The method for the determination of bismuth was that of Hanzlik and Mehrtens'[4] modification of Leonard's[5] method.

Bismuth was present in the spinal fluid of one of the two patients who had fever produced by malaria. Seventeen cubic centimeters of spinal fluid contained 0.01 mg. of the metal bismuth. In the patients

4. Hanzlik, P. J., and Mehrtens, H. G.: Clinical Excretion of Bismuth: Bismuth Metal, Arch. Dermat. & Syph. **22**:483 (Oct.) 1930.

5. Leonard, C. S.: Studies in Pharmacology of Bismuth Salts: Method for Determination of Bismuth, J. Pharmacol. & Exper. Therap. **28**:81, 1926.

who received fever therapy produced by diathermy, the spinal fluid did not contain bismuth. Bismuth was present in the spinal fluid of two patients who had received the Swift-Ellis treatment. The presence of bismuth in the spinal fluid of these two patients might be attributed in part to the bismuth contained in their blood serum which was injected subdurally as part of the Swift-Ellis treatment since the injected serum contained 0.04 mg. per hundred cubic centimeters. In the remaining two patients receiving the Swift-Ellis treatment, the spinal fluid did not contain bismuth. The Swift-Ellis treatment of these patients was purposely performed with the serum of other patients who were not receiving a bismuth compound; hence the injected serum did not contain bismuth. Bismuth was absent in the spinal fluid of the remaining patients in this group.

The second group comprised seventeen patients who were treated with sodium iodobismuthite. This bismuth compound was injected intramuscularly, twice weekly, in doses of 2 cc. (25 mg. of the metal bismuth). The majority of patients received from ten to fifteen consecutive injections; a few, six consecutive injections, and others as many as thirty consecutive injections. The amount of spinal fluid examined for bismuth ranged from 12 to 20 cc.; except for two patients the fluid withdrawn at different times was pooled, totaling 45 and 55 cc. respectively.

Bismuth was present in two of the seventeen specimens of spinal fluid examined. In one of the positive specimens 0.0015 mg. of bismuth was present in 22 cc. of spinal fluid. The patient from whom this fluid was obtained had optic atrophy and had received twenty-five Swift-Ellis treatments. In some of these treatments, hypertonic salt solution [6] was injected subdurally. The other positive specimen contained 0.0019 mg. of bismuth in 19 cc. of spinal fluid. The patient from whom this fluid was obtained had nine Swift-Ellis treatments, and in some of these treatments hypertonic salt solution was injected subdurally.

It is to be noted that bismuth was not found in the specimens totaling 45 and 55 cc. of spinal fluid.

EXPERIMENTAL STUDY

A total of thirty rabbits were given injections of five bismuth preparations: sodium iodobismuthite (iodobismitol), bismuth arsphenamine sulphate (bismarsen), potassium bismuth tartrate, bismuth salicylate and bismuth camphocarboxylate (bismocymol). Each of six rabbits received the same bismuth preparation. The dose was 3 mg. of the

6. From 1 to 2 cc. of a 10 per cent solution of sodium chloride was mixed with the serum injected subdurally.

compound per kilogram of body weight, injected intramuscularly. This dose is about twice the amount recommended for these compounds in man. The injections were given twice weekly, for thirteen, fourteen and fifteen consecutive injections. The animals were exsanguinated, and the entire brain removed for analysis. The brains weighed from 6.8 to 9.6 Gm., the average being about 8 Gm.

Bismuth was found in the brain of one of the six rabbits given injections of sodium iodobismuthite and in one of the six rabbits given injections of potassium bismuth tartrate. The brains in the remaining animals did not show the presence of bismuth.

The spinal fluid of the rabbits given injections of different bismuth compounds was not examined because of the small amount obtainable. Moreover, bismuth was more likely to be present in the brain than in the spinal fluid.

COMMENT

Our results are in agreement with those of the majority of investigators but are in conflict with the studies of Hanzlik and his collaborators who found a high incidence of bismuth in the spinal fluid of patients treated with sodium iodobismuthite and in the brain of guinea-pigs after injection of the same compound.

Our results furnish some evidence that the state of fever produced by malaria therapy of neurosyphilis, and also an aseptic meningitis as produced by the subdural injection of salt solution, rather than the patient's own serum, increase permeability of the nervous system for bismuth.

The spinal fluid contains more anions than cations; bromine and iodine, which are anions, readily penetrate into the spinal fluid. From these considerations, Mehrtens and Pouppirt [7] formulated the hypothesis that the ionic state of a metal in a compound is a determining factor in its penetration into nerve tissue. This suggested the employment of sodium iodobismuthite in which the bismuth (an amphoteric metal) exists as an anion. The fulfilment of this hypothesis requires, however, that the bismuth atom remain in the anionic form after the compound is injected into the organism. It should be recalled that few compounds retain their chemical integrity following introduction into the body. Only anions which remain as such under any condition, such as bromine and iodine, can be expected to act as anions after introduction into the body. Moreover, the majority of organic compounds are quickly disintegrated by chemical action of body tissue in vivo. No complex metallic derivative is known which does not undergo such disintegration after introduction into the body.

---

7. Mehrtens, H. G., and Pouppirt, P. S.: Anionic Bismuth Therapy in Neurosyphilis, Am. J. Syph. **16**:373, 1932.

The study of Hanzlik and his collaborators [8] on the excretion of sodium iodobismuthite has shown that the bismuth of this compound is excreted by the kidneys in a way comparable to that of other compounds in which bismuth is present. In their study there was evidence of hydrolysis at the site of injection of the compound.

These investigators assumed that cerebral penetration of bismuth will occur more readily if combined with iodine as in the compound iodobismuthite, since it is known that iodine readily penetrates the nervous system. This assumption is not tenable in view of the foregoing considerations and also in view of the well known fact that the salicyl anion of the compound bismuth salicylate, after injection into the body, appears in the spinal fluid, whereas the bismuth cation does not.

Our failure to determine cerebral penetration after injection of sodium iodobismuthite supports the belief that the bismuth of this compound, like that of all other bismuth compounds, is changed in the body to a stable salt and is excreted as such.

1934 Spruce Street.

2101 Pine Street.

8. Hanzlik, P. J.; Mehrtens, H. G.; Gurchot, C., and Johnson, C. C.: Iodobismitol: A Soluble Bismuth Product for Use in the Treatment of Syphilis; A Preliminary Report, J. A. M. A. **98**:537 (Feb. 13) 1932.

EPIDERMOMYCOSIS AND FLATFOOT

DAVID LIEBERTHAL, M.D.
AND
EUGENE P. LIEBERTHAL, M.D.
CHICAGO

In the past two and one-half years the most striking fact that we observed in a large series of cases of mycotic infection of the feet was the presence of an associated moderate to advanced degree of flatfoot. In reviewing the literature on the treatment of fungus infections of the feet we have failed to find any mention of this so frequently associated disturbance or of orthopedic measures to correct it. Of the one hundred and ninety-five patients in this series, 90 per cent had flatfoot. Thirty per cent also had hyperhidrosis. This high percentage of flatfoot in mycotic infections of the feet raised the question in our minds as to whether the resistance of these infections to therapy could not be explained in great measure by the changes caused by flatfoot. This seems highly probable when we review the mechanics of flatfoot. The first change that occurs in flatfoot is a relaxation and depression of the bony structures of the foot. This in turn exerts undue pressure on the softer structures below, such as the muscles, the tendons, the nerves and the arteriovenous and lymphatic systems. In the last case a diminished circulation occurs. It would be logical to assume that, as a result of these changes, the resistance of the skin itself is lowered, and the soil thus prepared for the invasion and subsequent growth of the fungi. The incorrect distribution of the body weight which is usually present in flatfoot may also cause the lesions of the skin to be subjected to undue trauma.

Ten cases in this series which presented advanced vesiculopustular lesions on the soles as well as intertriginous changes were highly resistant to all forms of treatment. Five additional cases which presented moderately advanced vesiculopustular lesions on the soles as well as intertriginous changes responded slowly to the ordinary forms of therapy. These fifteen cases, which were accompanied by flatfoot, were referred for orthopedic correction of the latter condition in the hope that the cutaneous lesions might be influenced favorably. The mycotic changes then began to respond more rapidly to the ordinary forms of treatment. Not only did the lesions of the skin clear up rapidly, but

the hyperhidrosis was also materially influenced. In three cases it disappeared completely. The rapid response of these resistant cases to the ordinary therapeutic measures following the correction of the foot deformity justifies the conclusion that orthopedic corrective measures are an important therapeutic adjunct in the cases of fungous infection of the feet which are associated with flatfoot.

104 S. Michigan Avenue.

URTICARIA

ETIOLOGIC OBSERVATIONS

J. G. HOPKINS, M.D.
AND
B. M. KESTEN, M.D.
NEW YORK

We know that an urticarial wheal can be produced in normal persons by the injection of histamine, morphine and innumerable other substances and also by localized mechanical, thermal or electrical injury. We also know that in patients with serum sickness, hay fever, asthma, and eczema the intradermal injection of the substances to which they are sensitized produces a wheal although these substances have no such effect on normal skin. The serum of allergic subjects will often locally sensitize the skin of normal persons so that it in turn will react to subsequent injection of the allergen or, in some instances, to absorption of the allergen after it is swallowed.

The investigations of Philippson, Lewis, Blackley, Prausnitz and Küstner, Walzer and others have established these facts and added greatly to our knowledge of the pathogenesis of wheals. There remains, however, a gap between our understanding of the mechanism of wheal formation and our information as to the causes of the general eruptions of wheals which we refer to as urticaria.

Urticaria is a symptom of many diseases. It occurs in serum sickness, asthma, hay fever and eczema, in anaphylactic shock and occasionally in leukemia cutis, dermatitis herpetiformis and other dermatoses.

Urticaria presents the problem that so often arises in the classification of dermatoses. If diagnosis is based on clinical morphology one must recognize that the same cause may produce in the same patient at one time an erythema, at another time an urticaria, at another time a vesicular eruption and at still another time an angioneurotic edema. This emphasizes the value of Osler's phrase, "The Erythema Group of Skin Diseases." In other cases the same excitant may cause both urticaria and asthma, and etiologically one must consider them one disease. Often, however, wheals are the only symptom or the dominant one, and in such instances it is customary to diagnose the condition as urticaria with the recognition that these cases do not form an etiologic entity.

From the Department of Dermatology, Vanderbilt Clinic, Columbia University.

Read at the Fifty-Sixth Annual Meeting of the American Dermatological Association, Chicago, June 8, 1933.

Determination of the etiology of urticarias varies greatly in difficulty. In some cases the cause is so obvious that the patient recognizes it without consulting a physician, in others it is so obscure as to escape detection after intensive study. These obscure cases are often the most prolonged and distressing and present a serious problem in diagnosis and treatment.

URTICARIA CAUSED BY CONTACT

It seems that some information as to obscure cases of urticaria might be obtained by examining the simpler cases whose etiology is well understood. The simplest examples are probably the urticarial outbreaks which follow contact with substances such as the poison of nettles or of certain caterpillars which uniformly produce urticaria on any person exposed, the eruption being limited to the area of skin in contact with the irritant.

Local urticaria is also occasionally produced by contact with substances which in the average person cause no reaction and which have not previously caused a reaction in the patient concerned.

E. D., a medical student, was assisting in a laboratory. After she held a cat for several hours, urticaria developed on the arms and was limited to the parts in contact with the animal. Previous frequent though less prolonged contact with cats had never caused hives. An intracutaneous test with cat hair gave a positive reaction; a percutaneous test gave only a questionable reaction.

This type of urticaria is rarely, if ever, mentioned in discussions on the etiology of the disease. We have seen 1 other case which seemed caused by sensitization to cosmetics and 3 cases in which the history indicated that flowers, Pyrethrum and hair dye were respectively the excitants, though we were unable to confirm this by tests. One of us has reported a case in which a generalized outbreak followed patch tests with orange peel.

There are two types of urticaria caused by contact: the toxic and the allergic. The former is produced by substances which have the pharmacologic property of producing wheals in normal skin. The latter is caused by substances which have no such special toxic action. The wheals result from some form of allergic reaction occurring only in the skin of sensitized persons.

The former group seems comparable in its mechanism to the wheals experimentally produced by histamine, morphine, etc.; the latter, to the wheals produced in performing cutaneous tests for allergy.

URTICARIA FROM INTERNAL CAUSES

In contrast to these localized urticarias caused by substances reaching the skin from without are the more numerous generalized urticarias in which the exciting substance arrives at the skin from within—pre-

sumably through the blood stream. Here again there is much to suggest the existence of two types of causative agents, one toxic, the other allergic.[1]

Many generalized urticarias, and in fact most of those of known causation, are allergic in the sense that they are reactions to stimuli harmless to normal persons. These will be grouped according to the nature of the causative agents. Other forms which show no relationship to allergy will be discussed later.

SERUM SICKNESS

Evidence that generalized urticaria results from an antigen-antibody reaction is clearest in the cases which follow the injection of horse serum. This evidence is completely presented in the contributions of Longcope and Rackemann [2] and of MacKenzie and Hanger.[3] A review of the salient and probably familiar facts may help to clarify our ideas as to other urticarias.

1. The intravenous injection of horse serum results in urticaria and other symptoms of serum sickness in many normal persons. The number attacked is roughly proportional to the amount of serum injected. Amounts of 100 cc. or more cause symptoms in about 90 per cent of patients. A few seem unaffected by any amount.

2. In normal persons the symptoms appear after a latent period, usually from six to twelve days, occasionally from two to three weeks.

3. The antigen (horse serum protein) can be detected in the blood for a period of from two to three weeks. In patients who react severely it disappears promptly. In those with no symptoms it persists for weeks or months.

4. Antibodies (precipitins) appear in the serum of patients after symptoms have developed, usually from the ninth to the twenty-first day. There are large amounts in patients who have severe symptoms and who quickly eliminate the antigen. Antibodies are absent or present in traces in patients who show no symptoms and who retain their antigen for a long time.

5. In certain patients previously treated with serum, in those with horse asthma and in others presumably sensitized, shock, accompanied by urticaria, occurs immediately after the injection of horse serum. In still other cases the symptoms of serum sickness appear after a diminished period of incubation of less than six days.

6. In patients with serum sickness a skin reactivity to horse serum usually develops during or after their illness. Patients who react with shock show a positive cutaneous reaction before the injection. (Exceptions to this rule have been reported.)

7. Hypersensitive persons may sometimes be desensitized by suitable small injections of the antigen.

---

1. Storm van Leeuwen, W.: Brit. J. Exper. Path. **3**:282, 1922.

2. Longcope, W. T., and Rackemann, F. M.: J. Exper. Med. **27**:341, 1918.

3. MacKenzie, G. M., and Hanger, F. M.: Serum Disease and Serum Accidents, J. A. M. A. **94**:260 (Jan. 25) 1930.

These facts indicate that in serum sickness urticaria results from the reaction of antigen still present in the body with antibodies developed in response to its injection. These antibodies react before they are demonstrable in the blood and presumably while still united with the cells in which they develop. The patients are not allergic at the time the serum is injected, but the subsequent development of these antibodies causes them to react with allergic symptoms. In persons allergic to horse serum such antibodies are probably present and ready to react at the time of injection, or the mechanism for their production is so prepared that they are produced with abnormal speed.

URTICARIA CAUSED BY FOOD

Probably the most familiar types of urticaria are those which are caused by eating specific foods. Among them are three groups which require separate consideration, although the differences between them may not be fundamental.

1. In some patients the urticaria is accompanied or followed by other symptoms indicating a general allergic reaction.

2. In others urticaria is the only symptom.

3. In still other patients in whom attacks regularly follow the taking of a certain food, urticaria also occurs from other stimuli. In these food can be considered only as a contributing or alternating cause of the urticaria.

Urticaria with General Food Allergy.—The only cases in our series belonging to the first group were those of 4 children.

J. L., a female infant, was a typical example. There was a history of asthma in her mother and in her father's family. Her mother and sister had urticaria caused by food. During the first three months of the infant's life, when she was breast fed, she had no allergic symptoms. After the first feeding of cow's milk a red rash developed about the mouth, and after three feedings a generalized urticaria with swelling of the eyelids which persisted for two or three days occurred. Stopping the feeding of milk prevented urticaria, but further attempts to give raw milk, boiled milk, lactic acid milk and evaporated milk were invariably followed by hives and several times by violent sneezing. The child gave a doubtful reaction to percutaneous tests with cow's and goat's milk, but large wheals with pseudopodia developed after intracutaneous tests with cow's milk, lactalbumin, lactoglobulin and egg albumin.

When the child was 5½ months of age desensitization was begun by the daily feeding of powdered milk, beginning with 2 mg. This was rapidly increased to 100 mg. in one week and to 4 Gm. in three weeks without causing symptoms. One-half ounce (15 cc.) of raw milk was then given and was followed by sneezing. The dose was increased to 2 ounces (60 cc.), which was refused. Then after forced ingestion of about 1 ounce an alarming attack of asthma lasting twenty-four hours developed, but no urticaria appeared. A week later desensitization was resumed with a dose of 15 mg. of powdered milk, the dose being increased more slowly. Slight asthmatic symptoms were noted at times but no urticaria, and after six months 120 Gm. a day was taken without symptoms. A trial of 2 drops of

evaporated milk was, however, followed by asthma and edema of the eyelids. Within a few days dry scaling patches of eczema developed on each cheek. These persisted for only a few weeks. The feeding of raw milk at this time again produced urticaria and angioneurotic edema.

Eleven months after beginning desensitization the intradermal reaction to milk was doubtful, and raw milk was fed again, beginning with 1 drop. In three months this was increased to 9 ounces (270 cc.) a day without inducing urticaria. The intradermal reaction became completely negative. The child then tolerated 1 quart (946 cc.) of milk daily.

When first observed this child gave a positive cutaneous reaction to egg though at that time the eating of eggs caused no symptoms. Later, however, after the attacks of asthma caused by milk, she began to have asthma whenever she ate eggs. This has persisted, but the sensitivity to milk has disappeared since the course of desensitization. We have followed her for three years, and she has had no allergic symptoms from milk.

Of the other 3 children, 1 had attacks caused by milk, the second, by eggs, and the third, by a number of various vegetables. In all, urticaria invariably followed the taking of the incriminated foods, and in none did it occur otherwise. All had other allergic symptoms due to the same foods. One child immediately vomited, and then asthma developed; the second vomited and coughed violently, and the third had suppression of urine probably owing to edema of the urethra. The children who were sensitive to eggs and milk gave positive reactions to these foods by intradermal tests, but percutaneous tests with the responsible foods produced negative reactions in all. A family history of allergy was obtained in 1 case; it was absent in the second and was not recorded in the third.

Similiar instances of urticaria and asthma or of intestinal allergy in adults are familiar, though they were not encountered in our series. It appears that hives or vomiting is often the first symptom, but that in older persons asthma becomes more severe and dominates the picture.

There seems to be no doubt that these cases are instances of allergy to the foreign protein of foods and comparable to the immediate reactions to the injection of horse serum. In fact, it was in 2 such cases of urticaria caused by eggs and fish and associated with asthma that Walzer and Walzer [4] demonstrated the reaction of passively sensitized areas of the skin of normal persons to ingestion of these foods.

In all our cases symptoms followed the first taking of the responsible food, and in few of the recorded cases there is evidence as to how the sensitization was brought about. However, in the case described and in those reported by Schofield, Schloss and others, desensitization was accomplished.

---

4. Walzer, A., and Walzer, M.: Urticaria: Experimental Wheal Produced on Normal Skin Through Internal Channels, Arch. Dermat. & Syph. **17**:659 (May) 1928. Walzer, M.: J. Immunol. **11**:249, 1926.

Urticaria Caused by a Specific Food.—Undoubtedly the most common form of generalized urticaria is that occurring in repeated acute attacks unaccompanied by other symptoms and following the taking of a specific food. Such patients seldom consult a physician as the causation is evident to them from the sequence of events.

A woman, aged 34, stated that twenty years before, on eating shrimps for the first time, hives developed, and that on ten or more occasions the eating of this shell-fish had been followed by attacks.

She had never eaten shrimps without having an attack. She believed that if she took alcohol at the same time the outbreaks were far more severe. At first the hives appeared all over the trunk and extremities. Later they were usually limited to the hands and face. They began within an hour after she ate the shrimps, and successive lesions appeared for the following twelve to twenty-four hours. In one attack which occurred shortly before she was seen, hives recurred every evening for three weeks. There were no intestinal or other symptoms. Repeated scratch tests and one intradermal test with shrimps during and following an attack gave negative reactions.

The patient recalled no attack of generalized urticaria except after eating shrimps, though occasionally she had a few scattered hives from an unknown cause. She had no other allergic symptoms. There was, however, a marked history of allergy in the family. Her two brothers, her mother, a maternal aunt, her maternal grandmother and two maternal great aunts had hay fever. Her two sisters and two maternal aunts had urticaria, and her mother suffered from migraine.

In our series of 200 cases there were 13 adults in whom the history and course of the eruption led us to conclude that the attacks were due solely to reactions to specific foods. In most instances this conclusion was based solely on the history. Ten of these patients had recognized the cause of their attacks. The remaining 3 came to us complaining of hives of unknown cause, and their reaction to food was detected by cutaneous or dietary tests.

Eleven of the patients were tested with the various foods which had caused their urticarial outbreaks. Eighteen such tests made by the percutaneous method gave negative reactions. Of fourteen intracutaneous tests, four were positive, two doubtful and eight negative.

Urticaria with Food as a Contributing Cause.—In addition to the cases just described in which the occurrence of urticaria seemed entirely explained by the ingestion of specific foods, there were other patients (4 children and 11 adults) for whom the picture was less clear. Two gave the curious history that certain foods caused urticaria if they were subsequently exposed to cold. One of these patients worked in a meat market and found that after eating beef or pork he broke out with hives on entering the icebox. At other times entering the icebox caused no trouble nor did eating of these foods do so if he was not exposed to cold. Merklen has reported similar cases.

The other 9 patients all stated that an attack followed the taking of some unusual food or that repeated attacks followed ingestion of a food which they used only occasionally. They did not, however, remain free from attacks even while abstaining from these foods, and after an outbreak excited by food hives of more or less severity continued to appear for a period of weeks or months, gradually subsiding. In an infant who had eaten tomato for the first time a severe outbreak of hives occurred, and following this other foods which the patient had eaten previously without injury also caused attacks of hives.

Pathogenesis of Urticaria Due to Food.—In the first group of cases described we are evidently dealing with an expression of allergy of the familial type. A wheal indistinguishable from the spontaneous lesions can usually be produced in these patients by injecting into their skin the food substance to which they are sensitive, and antibodies in their serum can be demonstrated by passive transfer. They can frequently be desensitized.

In patients of the second group the intradermal injection of a food which regularly causes urticaria when taken by mouth usually produces no reaction whatever. It seems a paradox that a patient with eczema or asthma caused by food will usually respond with an urticarial wheal to the injection of the causative agent into his skin, but that a patient with urticaria from food—unless he has also some other allergic symptoms from food—will rarely give such response. This indicates that if, as seems probable, urticaria from food is due to a reaction between antigen and antibody, the reaction does not take place in the skin. A discussion of the interesting problem of its mechanism would exceed the scope of this report.

Doubtful Cases of Urticaria Due to Food.—So far we have considered only cases in which the history leaves little doubt as to the relationship of urticaria to the ingestion of a specific food. The outbreaks occurred within an hour or two of taking the food, even if minute amounts were ingested, and in most instances the attacks were transient. The studies in serum sickness indicate that a reaction due to food need not present these characteristics. If we accept the two conditions as analogous we must consider the possibility that in an unsensitized person food might cause urticaria only in excessive amount and only after lapse of sufficient time for the development of antibodies (from six to twelve days), and that in those not acutely sensitized there might be a period of incubation of one or two days. We have seen cases in which food taken one or two days before the attack was suspected of being the cause. As to foods taken the previous week, it is difficult to fix even a suspicion. The possibility that they were the cause must, however, be admitted and might help to explain the large

number of undiagnosed cases. We have also observed cases in which urticaria following excessive eating of fish by persons who had taken moderate amounts without symptoms or in which urticaria followed general overeating. Such occurrences seem to be in harmony with what we know about serum sickness.

The prolongation of symptoms is sometimes difficult to explain. In the typical case of urticaria caused by shrimps which we have described, one attack lasted ten days. This could be explained as due to retention of the antigen such as is known to occur in serum sickness. Frequently, however, an urticaria believed to be caused by food persists so long that it could hardly be explained as due to persistence of the foreign protein within the body.

TABLE 1.—*Foods Causing Urticaria (Proved and Probable)*

				Results of Tests			
				Percutaneous		Intracutaneous	
		Age					
Foods (27)	Total	Child, Under 12	Adult, Over 12	No. of Patients Tested	No. of Patients with Positive Reaction	No. of Patients Tested	No. of Patients with Positive Reaction*
Egg	8	7	1	8	3	4	1
Milk	6	5	1	6	1	5	2
Fruit †	16	6	10	14	0	8	0
Vegetables ‡	13	6	7	12	1	8	2
Fish §	4	0	4	4	0	3	0
Shell-fish ‖	4	1	3	3	0	1	0
Meat ¶	2	0	2	2	0	2	1
Chocolate	1	1	0	1	0	1	0
Total	54	26	28	50	5	32	6

* A wheal larger than controls with definite pseudopodia was regarded as a positive reaction.

† The positive reactions to fruits were: strawberry, 6; orange, 2; grapefruit, 2; lemon, tangerine, peach, pear, cherry and olive, 1 each.

‡ The positive reactions to vegetables were: tomato, 5; potato, mushroom, lima bean, onion, beet, radish, asparagus and group of vegetables, 1 each.

§ The positive reactions to fish were: cod, 2; sole and anchovy, 1 each.

‖ The positive reactions to shell-fish were: shrimp, 2; crab and clam, 1 each.

¶ The positive reactions to meat were: chicken and pork, 1 each.

For example, a patient stated that his urticaria began immediately after eating herring and persisted for three months. Another patient's urticaria began the night after a Thanksgiving dinner and persisted for a month. Another patient had urticaria for ten weeks following a fish dinner.

All this suggests that a reaction to food may set in motion a chain of events which are not at all understood but which in some way produce repeated outbreaks of urticaria. A possible explanation is the so-called anamnestic reaction—the effect of an acute reaction to one antigen in awakening a sensitivity to other antigens which has long been dormant. We previously reported the case of a boy who after an acute reaction to ringworm developed urticaria and eczema from milk, a food

which had caused him to have eczema in infancy but of which he had long been tolerant. Cleveland White [5] has described similar cases.

Another observation which we cannot explain is mentioned in the comment on the unclassified cases. A number of times a long-standing case of urticaria cleared up in a fairly convincing manner after the patient was placed on a restricted diet, and it seemed as if a reaction to one of the excluded foods explained the urticaria. On returning, however, to an unrestricted diet these patients failed to have a relapse. It seems necessary to suspend judgment as to whether food is the cause of urticaria in these cases until our diagnostic methods are improved.

URTICARIA CAUSED BY DRUGS

The urticarial eruptions frequently seen after the taking of certain drugs seem similar in all respects to cases of urticaria due to food, except that the substance causing them is not a protein and is not known to be antigenic. It is doubtful whether they differ in principle from the erythematous toxicodermas caused by drugs. Certain drugs such as cinchophen seem especially apt to cause urticaria. In most instances, as in most of similar urticarias from food, there is no history of the patient's having been sensitized. In the majority of cases caused by arsphenamine, however, the eruption does not occur until several injections have been given without any such effect.

Only 4 cases of urticaria from drugs were observed in this series. Two patients had repeated outbreaks following the taking of phenolphthalein; the others had attacks after injections of arsphenamine and neoarsphenamine. In 1 of the latter the urticaria was a fixed eruption. Hives recurred in identical areas during each injection or a few minutes later. After many such reactions in the circular areas from 3 to 8 cm. in diameter a dark pigment developed which persisted for nearly a year after the injections were discontinued. At first the reactions caused only discomfort from itching, but later symptoms of shock appeared which increased in severity until it seemed wise to abandon the treatment.

URTICARIA FROM INHALANTS

The frequent association of urticaria with asthma suggests that the exciting agent may be absorbed through the respiratory instead of through the gastro-intestinal tract. Walker has described urticaria as a complication of hay fever, and Brown has described a case accompanying dust asthma. Three of our patients had urticaria during asthmatic attacks but not at other times.

---

5. White, C., and Taub, S. J.: Sensitization Dermatoses of Nonfungous Nature Following Superficial Fungus Infections ("Ringworm") of Extremities, J. A. M. A. **98**:524 (Feb. 13) 1932.

G. R., a young man, gave cutaneous reactions to ragweed, cat hair, rabbit hair, several furs, house dust and several molds. For five years he had had attacks of asthma accompanied by urticaria. Both asthma and urticaria were apparently due to inhalation of dust constituents, but other factors, exertion or food, were not absolutely excluded.

Altogether the evidence as to urticaria from inhalants is surprisingly scanty and uncertain. Peters [6] informs us that urticaria rarely, if ever, occurs in purely inhalant-sensitive persons.

ABSORPTION THROUGH THE CONJUNCTIVA

In 2 cases it seemed probable that the antigen was absorbed through the conjunctiva, though the possibility of reaction from contact with the skin was not excluded.

T. L., a woman, aged 33, gave an interesting history of attacks of conjunctivitis accompanied by generalized urticaria which had recurred every July or August for twenty-eight years. She gave a factitious urticarial response to fifteen intradermal tests, and the pollen or other substance which caused these attacks could not be identified.

In a boy, aged 4 years, there developed on Easter day a conjunctivitis of the right eye with urticaria of the surrounding skin. A white rabbit hair was removed from the eye, and the symptoms promptly subsided. An intradermal test with extract of rabbit hair gave positive results.

URTICARIA FROM BACTERIA AND FUNGI

Urticaria Caused by Bacteria.—In 1907 Lustgarten and Winfield [7] simultaneously reported cases of urticaria and angioneurotic edema due to gallstones. Since then numerous reports have appeared of cases due to infected teeth, tonsils, sinuses, appendixes and gallbladders. Blumer and Rackemann described urticaria due to acute tonsillitis or sore throat. In general, focal infection has received only casual mention as a possible cause of urticaria, but Haldin Davis and Barber [8] insisted on its importance.

Barber said: "I am now inclined to believe that in the majority of patients in whom chronic or recurrent urticaria, with or without angioneurotic edema appears for the first time in adult life, the underlying cause is sensitization to bacterial rather than to food protein."

The extreme point of view is presented in the astonishing report of Menagh,[9] who stated that in 60 per cent of his cases of urticaria there was infection of the biliary tract and that in 49 per cent no other

6. Peters, F. H.: Personal communication to the authors.

7. Lustgarten, and Winfield, J. M.: J. Cutan. Dis. **25**:216, 1907.

8. Barber, H. W.: Brit. J. Dermat. **35**:209, 1923.

9. Menagh, F. R.: Etiology and Results of Treatment in Angioneurotic Edema and Urticaria, J. A. M. A. **90**:668 (March 3) 1928.

etiologic factor could be found. Of the latter, 88 per cent showed improvement or cure after treatment of this focal infection.

In the present series there were 8 patients whose urticaria cleared up completely after the removal of foci of infection.

In a children's nurse, aged 35, a sudden swelling of the left side of the face and numbness along the jaw developed following the filling of several teeth. This mass disappeared and a similar one appeared on the right side. For the ten weeks following similar swellings characteristic of angioneurotic edema continued to appear on different parts of the face. On roentgen examination two of the recently filled teeth appeared pulpless and showed evidence of periapical infection. These were extracted, and the angioneurotic edema disappeared.

Other cases of generalized urticaria followed a similar course.

A woman, aged 45, had an eruption of four weeks' duration. The hives were most severe on the buttocks and thighs, but occurred also all over the trunk and extremities. The individual lesions lasted an hour or two and seemed to recur in the same spots. They were most numerous and severe on waking in the morning, but a few were nearly always present. The itching was a torment.

For over a year she had been under great anxiety and physical strain on account of her husband's illness. Her sleep was frequently interrupted, and she had become increasingly fatigued until the slightest task was an effort. A month before the onset of the urticaria an abscessed tooth was removed, and following this she had an acute suppuration in one antrum. This had continued to drain, but she had been too busy to continue treatment. At about the same time she had an attack of abdominal pain with vomiting and diarrhea which was called intestinal grip. During the outbreak of urticaria she continued to have occasional attacks of diarrhea.

She had had repeated inflammations of the antrum previously, and six years before an unexplained acute urticaria which subsided in a few days.

After some ineffective efforts at symptomatic treatment the antrum was irrigated and much pus obtained. Following this there was an explosive outbreak of the urticaria, but with continued irrigations, in the course of a week the eruption completely disappeared. The fatigue and other symptoms promptly improved. For eighteen months there has been no recurrence of either the sinusitis or the urticaria.

We have listed in table 2 these and 12 other cases which seemed to respond to the treatment of focal infections. All these cases were chronic, and 7 of the patients had outbreaks nearly every day over a prolonged period. Five had other allergic symptoms, and 4 gave a history of allergy in the family.

A question of interest is whether or not these urticarias were due to sensitization to the bacteria in the lesions. The bacteria were not identified in most cases. However, it seemed significant that 12 of the 14 patients reacted to Staphylococcus aureus—either to an extract of the organism or to its soluble toxin (table 2).

Such reactions were also obtained in 31 of our undetermined cases. Many of these patients had focal infections, the relationship of which to the urticaria was unproved. Three who were treated subcutaneously with staphylococcic toxin remained practically free from lesions as long as the injections were continued. On the other hand, a reaction to the staphylococcus was rarely observed in the cases of urticaria known to be caused by food.

Urticaria Caused by Fungi.—A. P., who had been free from attacks for some weeks, on being tested with extracts of Mucor and Trichophyton broke out within a few minutes with a generalized urticaria which persisted for twenty-four hours.

TABLE 2.—*Urticaria Due to Focal Infection*

Case	Age	Sex	Duration	Location of Focus	Evidence as to Etiology	Reaction to Staphylococcus*	
						Immediate	Late
1	32	F	4 mos.	Teeth	Urticaria ceased after extraction.....	0	0
2	38	M	5 wks.	Teeth	Urticaria ceased after extraction.....	+	?
3	55	F	2 mos.	Teeth	Urticaria flared up and then ceased after extraction	+	+
4	64	F	8 mos.	Teeth	Urticaria ceased after extraction.....	+	+
5	35	F	7 wks.	Teeth	Urticaria ceased after extraction.....	+	+
6	50	F	2 wks.	Teeth	Urticaria ceased after extraction.....	0	?
7	35	M	4 wks.	Teeth	Marked improvement after extraction...	+	0
8	45	F	4 wks.	Sinus	Urticaria flared up and then ceased after drainage and irrigation	..	..
9	20	F	8 yrs.	Sinus	Repeated remissions after drainage and irrigation; improvement under injections of staphylococcus toxin †	+	+
10	25	M	1 yr.	Sinus	Remission after irrigation; improvement under injections of staphylococcus toxin	+	+
11	37	M	2 yrs.	Sinus and tonsils	Improvement after sinus drainage †.....	+	+
12	39	F	2 mos.	Kidney and bladder	Urticaria gradually cleared up after nephrectomy and irrigations of the bladder	..	..
13	42	F	4 wks.	Bladder	Urticaria ceased after irrigation of the bladder	+	+
14	10	M	3 mos.	Furuncles	Urticaria ceased when furuncles cleared up	?	+

* An immediate reaction consisted of a wheal with definite pseudopodia; a late reaction, of erythema 3 cm. or more in diameter in twenty-four hours.

† Cases 9 and 11 showed late reactions to toxin of Streptococcus haemolyticus.

Later eczematous patches developed at the sites of injection, indicating that the patient was sensitized to these fungi. This seemed to prove that fungi can produce urticaria under artificial conditions.

Evidence as to spontaneous attacks was difficult to obtain. Numerous cutaneous tests (about 500 altogether) revealed sensitization to one or more fungi in 25 cases. One patient reacting to Monilia albicans improved greatly after attempted desensitization to this fungus. Another patient with asthma and eczema as well as urticaria, who reacted to a dust mold (Trichothecium), was free from all symptoms while living in the country and had a relapse on returning home. In no case, however, could we prove that sensitivity to a fungus was responsible for the urticaria of which the patient complained.

URTICARIA CAUSED BY COLD, HEAT AND LIGHT

Urticaria from Cold.—The occurrence of urticaria on exposure to cold has long been noted. Harris, Lewis and Vaughan [10] studied its mechanism and its association with paroxysmal hemoglobinuria in patients with congenital syphilis. They transferred the sensitivity to the skin of other syphilitic persons by injection of the patients' serum and showed by experiments on absorption that the sensitizing substance is distinct from the hemolysin in the latter group of patients.

We observed 2 cases of urticaria in which cold seemed the only inciting cause.

R. D., a girl, aged 18, during the preceding winter noted for the first time outbreaks of hives on the parts exposed to cold when she went out of doors. On reentering a warm house the eruption vanished. During the summer she had attacks if chilled by bathing but not at other times. With cold weather frequent outbreaks again occurred. On testing we found that immersion of one arm in water at 80 F. produced an erythema, and immersion at 75 F. produced hives on the cooled area after seven minutes. After the arm was warmed for ten minutes the wheals disappeared. Immersion of the arm at lower temperatures or a full bath at 85 F. for ten minutes caused generalized urticaria.

F. W., a girl, aged 15, who had a severe coryza in the autumn, began to notice hives on exposed areas after being out in the cold. This urticaria continued during the winter. On testing, it was found that local urticaria appeared on immersion of the arm for three minutes at 66 F.

An attempt was made to desensitize her to cold; this seemed partly successful. She began with daily baths at 85 F. for two minutes. The temperature was then decreased until a bath at 64 F. for two minutes produced a severe attack. She began again at 66 F. for one minute and increased the exposure gradually to ten minutes. This again caused wheals. She continued, however, with moderately cold baths, and the following winter she had no urticaria except a brief outbreak which developed on going out in the cold after recovering from coryza.

It has been noted that cold seems to incite wheals in certain persons whose reaction to food is insufficient of itself to produce them. This may easily lead one into assigning to cold an urticaria that is essentially a reaction to food and controllable by diet.

In M. K., a girl, aged 9, with eczema from food, cold and food seemed alternating causes of urticaria. For five years she had frequent outbreaks which disappeared on restricted diet except for attacks which occurred after swimming in the summer or after exposure to cold air in the winter.

Urticaria from Heat.—Duke has described two types of urticaria from heat. In the first and more common type the application of heat to the skin causes a local outbreak of wheals. In the second, any factor which raises the temperature of the body—external heat, exertion or excitement—causes a more or less generalized eruption of atypical wheals.

10. Harris, K. E.; Lewis, T., and Vaughan, J. M.: Heart **14**:305, 1928.

Two cases in our series seemed to fall in Duke's second group:

M. L., a boy, aged 19, had attacks for five successive summers, beginning on August 1 and ending with cold weather. The individual outbreaks were associated with becoming overheated.

R. W., a man, aged 21, told a more circumstantial story. Two summers before while painting a house in the sun he became overheated; his face became red and covered with blotches which itched. After that physical exertion or nervous excitement caused an outbreak of red patches on the face and trunk and of hives surmounted with vesicles on the arms. Such an attack developed while he was waiting to be seen on his first visit to the clinic. As in Duke's case, his temperature was usually subnormal. After he took exercise while wrapped in blankets his temperature rose 2 degrees, and the urticaria appeared. Immersion of his arm in hot water had no such effect.

Urticaria from Light.—Urticaria due to sensitization to light was recognized by Merklen and has been carefully studied by Duke. We have recognized no examples in our series.

URTICARIA DUE TO ANIMAL PARASITES AND TO BITING INSECTS

Animal parasites contain substances to which man readily becomes sensitized. Urticaria has been recognized as due to Echinococcus, Ascaris and other intestinal parasites. Debow believed that fluid of Echinococcus cysts contained an urticariogenetic poison, but the observations of Rackemann and Stevens indicate that the reaction is due to allergy.

An urticarial wheal seems the normal response to the bite of many insects. In fact, the reaction is apt to be more severe in persons not previously exposed. Bullous reactions to stings of mosquitoes are observed in immigrants from Northern Europe and intense wheals from the bites of bedbugs in Negroes just arrived from the West Indies.

URTICARIA FROM METABOLIC CAUSES

Török stated the belief that jaundice, renal disease, gout and muscular rheumatism cause urticaria, and many authorities from Dühring to Pulay have accused uric acid. Lindberg could induce exacerbations in his patient by feeding nuclei acid. Wright found that large doses of calcium diminished urticaria and that the ingestion of citrates increased it. His theory that deficiency of calcium caused the eruption has had some supporters. His belief that the calcium in the blood was lowered was probably due to an inaccurate analytic method. Most later investigators have found the amount of calcium in the blood to be normal. More recently Keining and Hopf [11] have made observations similar to

11. Keining, E., and Hopf, G.: Deutsche med. Wchnschr. **57**:181 (Jan. 30) 1931.

Wright's, but have given them a different interpretation. They believe that a disturbance of the balance between inorganic bases in the tissues occurs in urticaria. Evidence of this is at present vague and difficult to evaluate. In any case, such a disturbance could not be the primary cause of urticaria but rather a step in its pathogenesis.

The apparently established fact that absorption of hematomas sometimes causes urticaria indicates, at least, that substances formed in the tissues can produce this eruption. Our own cases were not studied as to possible metabolic causation.

ENDOCRINE URTICARIA

Geber [12] studied patients whose urticaria occurred with each menstrual period and found that blood withdrawn during the attack would produce urticaria if injected intravenously. These results were confirmed by Lichter. Harrison [13] has obtained local and general reactions by the injection into such a patient of an extract of her own menstrual blood. Continued injections were followed by cessation of the urticaria. One example was observed in this series.

A married Negress, aged 27, had recurrent edematous swellings of the eyelids, lips, hands or feet and generalized urticaria for over two years. Outbreaks of one or of both of these conditions occurred nearly every month, during or a few days before the menstrual period. They subsided in two or three days, and at other times she was free. Except in the periodicity there was nothing to distinguish the eruption from the usual acute recurrent urticaria with angioneurotic edema. The patient had had asthma in infancy and her father had asthma; otherwise the history and physical signs seemed irrelevant.

Intradermal injection of her own blood serum withdrawn the day before menstruation produced an inflammatory papule within twenty-four hours. Serum taken during the menstrual period had no such effect. She has had no attacks for three months after a series of such injections.

We could find no definite evidence in any other cases that the urticaria was caused by endocrine disturbance.

Kaposi believed sterility to be one of the causes of urticaria. Levi and Rothschild, Ravitsch and others have ascribed cases to hypothyroidism. Pulay believed that some are caused by overactivity of the thyroid. A number of our cases showed evidence of thyroid disturbance, but we could not connect this with the urticarial symptoms.

We were impressed by the fact that the majority of our patients were women, and that a large number of them were at about the age of the menopause. We have seen severe urticaria follow artificial meno-

12. Geber: Dermat. Ztschr. **32**:143, 1921.

13. Harrison, W. T.: Case of Menstrual Allergy, J. A. M. A. **100**:738 (March 11) 1933.

pause produced by radium, but we could not ascertain whether there was any causal relationship.

A case that impressed us as probably due to ovarian disturbance was that of a woman, aged 52, who for two years had the most persistent, severe and distressing urticaria and edema which we observed. The lesions varied in intensity from hour to hour and from week to week, but she was rarely free. There were regular nightly exacerbations and periods of four or five days when the swelling of the face or of the hands and feet was disfiguring and disabling. At times edema of the epiglottis and throat prevented her swallowing anything but fluid. At times she was confined to bed in great distress from the pruritus. She had attacks of abdominal pain and vomiting and of typical ureteral colic for which no other cause than the urticaria could be found.

She had no other allergic symptoms. Intradermal tests to food and contact substances gave negative results, and similar tests done elsewhere had shown no reaction except to bacon. Various elimination diets were tried thoroughly without relief. Sensitization to food seemed excluded.

This patient had previously had an ovarian abscess which had been treated surgically. While under observation she had abscessed teeth, acute otitis media, maxillary sinusitis and cystitis. She gave a strong immediate and late reaction to extracts of Staph. aureus. However, extraction of the teeth and apparently successful treatment of the other infections and attempted desensitization to the staphylococcus toxin had no effect on the urticaria. We could not prove that these infections were related to it. The taking of epinephrine and ephedrine sometimes gave temporary relief. Calcium, orally, intramuscularly and intravenously, parathyroid extract-Collip, autohemotherapy and colonic irrigations had no definite effect, though temporary relief was recorded.

Fourteen months after the onset of the eruption her menses, which had been regular but very painful, ceased. The urticaria continued. After an absence of four months she returned and stated that she had been taking 15 grains (0.97 Gm.) of ovarian extract daily and had had no hives. This may, of course, have been mere coincidence, but we followed her up another year under continued ovarian therapy, and she had only one mild attack.

CONSTIPATION

The majority of our patients with chronic urticaria were constipated. This is, however, such a common and unmeasurable complaint that its significance is doubtful. Eyerman [14] has demonstrated by roentgenography colonic stasis during attacks of urticaria, and it is possible that constipation is the effect of the urticaria rather than the cause.

It has been suggested that the absorption of histamine from the intestine might cause urticaria, but there are few facts to support this hypothesis. Meakins and Harrington reported the finding of histamine in the cecum and in the ascending colon. Longcope believed that histamine or allied substances absorbed from the bowel were a probable cause of renal insufficiency. Lieb [15] reported a case of epilepsy and

14. Eyerman, C. H.: J. Missouri M. A. **24**:129, 1927.

15. Lieb, C. W.: New York State J. Med. **24**:847 (Feb. 1) 1924.

urticaria as resulting from such absorption. Certainly the belief that urticaria may be caused by toxic substances absorbed from the colon is frequently expressed by writers on urticaria and on constipation, though it rests on insecure grounds.

From analogy with cases known to be due to focal infection, it would seem that sensitization to bacteria in the intestine might explain some urticarias. Our associate, Dr. Lyons, demonstrated sensitization to Bacillus coli in a patient whose urticaria was associated with digestive disturbances and constipation.

The evidence from therapeutics is uncertain. Temporary subsidence of urticaria frequently occurs after the bowel is emptied. We have seen many chronic cases improve and a few clear up after colonic irrigations, a diet low in protein, the ingestion of acidophilus milk and similar therapy, or after an anticonstipation regimen. In more instances such treatment has been without effect. However, we should recommend such methods to the unfortunate physician confronted with the necessity of doing something though he has no logical grounds for doing anything. They seem as likely to help and far less apt to do harm than injections of calcium, milk, peptone, horse serum or the patient's own blood, procedures which are equally irrational.

PSYCHOGENIC URTICARIA

Urticaria has been said to be produced by suggestion or autosuggestion, and many cases have been ascribed to emotional stress or shock. Hardy and, later, Rapin reported that after they had lectured on urticaria one of their auditors broke out with hives. Wright asserted that a patient of his, a physician, could produce an outbreak at will. Reports of cases due to psychic stimuli of various types have been collected by Merklen and Cassirer and more recently by Flandin.[16] Hartzell's case of the boy who broke out with the hives whenever addressed by strangers is a good example.

In the case of a Jewish spinster, aged 36, we were almost forced to believe that the urticaria was psychogenic. She was constitutionally inferior and had a low intelligence quotient. The psychiatrists concluded that she had "a psychoneurosis of the conversion type with elements of both anxiety and neurasthenia." For four months she had urticarial outbreaks whenever she was emotionally disturbed, e. g., after quarrels with her landlady, after disappointments in love and after visits to friends whom she envied because they were happily married. When not emotionally disturbed she was free from urticaria.

Indications of a relationship between emotional upsets and urticaria were obtained in other cases. One young woman broke out from head to foot when told of an injury her brother had sustained in a motor accident. A young matron always had hives when her husband brought strangers to dinner. However, the majority of these patients also had

16. Flandin, C.: Bull. et mém. Soc. méd. d. hôp. de Paris **50**:1264, 1926.

hives without any known emotional stimulus. One can never make certain that the emotional stress did not merely exaggerate or set off an outbreak due to some physical cause. Török suggested that Duke's observations on urticaria from heat may offer an explanation for many apparently psychogenic cases. It is easy to assume a psychologic basis for phenomena the physical cause of which is difficult to detect.

CLASSIFICATION OF CASES STUDIED

We have attempted to group under the foregoing heading some 200 cases studied in the allergy class of the dermatologic clinic during the past five years. Cases of urticaria from contact are as a rule too trivial to need medical attention. Patients with simple urticaria due to food usually recognize the cause of their symptoms and seldom apply to a clinic for relief. Patients with urticaria from drugs or urticaria associated with asthma are usually under the care of an internist. Consequently the small proportion of such cases in our series is misleading.

TABLE 3.—*Number of Cases in Which the Cause of Urticaria Was Determined*

	Proved	Probable
External contacts	..	2
Food (in patients with other symptoms of food allergy)	9	13
Food (in patients without other symptoms of food allergy)	3	15
Food a contributing cause	..	6
Drugs	5	1
Substances absorbed through the conjunctiva	..	2
Bacteria	..	14
Heat	1	3
Cold	2	1
Menstruation	1	..

Cases in which the attacks could be reproduced or in which there was reliable evidence of repeated attacks after the same stimulus are listed as "proved." Cases in which the patients were free from attacks after avoidance of food or drugs or after removal of foci of infection have been listed as "probable." We have included with the latter cases a few in which the major attacks stopped, although trivial outbreaks probably due to some other factor recurred.

Undetermined Cases.—We should be chagrined to admit inability to determine the etiology in such a large proportion of cases, did we not believe this to be a common experience.

In 193 of 214 cases studied we were unable to reach any definite conclusion as to the cause of the urticaria. In about one third of these we could assign our failure to insufficient observation, but others were observed for months and the patients cooperated in all the tests undertaken. Of the 139 patients, 44 showed sufficient improvement on elimination diets to suggest that food was a causative factor. Twenty had foci of infection which were not cleared up under treatment, so that the

relationship of such foci to the eruption remained doubtful. There remained 75 cases in which we could find no evidence of food allergy, focal infection or other factors known to cause urticaria. Among these were the cases in which we have commented on the possibility of endocrine or psychic origin.

This experience suggested two probabilities. First, that in patients subject to urticaria various stimuli may at different times excite attacks. This seemed true of the cases for which we listed food as a contributing cause. It seemed probable also that among our undetermined cases those in which the patients improved on restricted diet but still had minor outbreaks and those which responded similarly to treatment of focal infections were cases of multiple etiology.

The second probability is that some urticarias of internal origin, like some of those due to external contact, are not allergic. Of the 12 patients with definite urticaria from food, which is presumably allergic, 9 (75 per cent) had other allergic symptoms and 8 (66 per cent) gave a history of allergy in the family, whereas of 57 patients with no suggestion of dietary or bacterial cause and of whom the record was adequate, only 10 (18 per cent) had other allergic symptoms, and of 48 such patients, 17 (35 per cent) gave a history of allergy in the family. In these undetermined cases we were dealing less frequently with obviously allergic persons.

This suggests that there are causes of urticaria, possibly toxic, metabolic or endocrine or possibly purely psychic, which as yet we are unable to determine.

CLINICAL CHARACTERISTICS

It is interesting to review the characteristics of cases known to be due to different causes to see whether one may detect clinical signs which point to one or another etiologic factor. It seems useful to divide urticarias into those which occur as acute attacks, usually recurrent at longer or shorter intervals, and the chronic forms in which hives appear frequently over long periods. One may also distinguish between generalized and localized forms. It must be admitted that such distinctions are arbitrary and difficult to make in some cases.

Localized urticaria was produced by chemical or physical agents reacting by contact with the skin, but also in some instances by food and in one case apparently by reaction through the conjunctiva. Symmetrical urticaria in acral distribution was due to cold.

Acute generalized outbreaks repeated at considerable intervals were caused by specific foods or drugs rarely taken. The attacks caused by drugs were in general of shorter duration. Similar attacks may accompany asthma. Single attacks of acute urticaria may be caused by an unaccustomed food or drug, but also apparently by infections and quite possibly by other factors.

Beyond this, conclusions seem less certain. The chronic generalized urticarias are rarely due solely to food or drugs, though 2 cases due to eating of eggs showed almost daily outbreaks. In at least 6 other cases of chronic hives specific foods seemed to bring on exacerbations.

The point of greatest interest to us was that some of these chronic cases were due to focal infection. In fact, those shown to be due to focal infection were the only typically chronic cases that we could completely explain.

Diagnosis.—The history taken with patience and discrimination is the most helpful means of diagnosis in urticaria. Of our 39 cases of urticaria from food the cause was stated in the history in 30. In fact, unless some clue was obtained by questioning the patient, we were seldom able to determine the etiology.

Cutaneous Tests.—Cutaneous tests with foods are of little practical value in urticaria. In only 10 per cent of the cases in which there was little doubt as to the causative food was a definitely positive test with this food obtained. These reactions are summarized in table 1. It will be seen that the intracutaneous method gave 20 per cent of positive tests in such cases; the percutaneous, only 10 per cent. Altogether about 1,300 percutaneous and 3,000 intracutaneous tests with food were made in the 214 patients studied; in only 2 cases were such tests of decisive help in the diagnosis, and in 1 of these the percutaneous tests served only to mislead us.

M. O'D., a woman, aged 35, had intermittent attacks of generalized urticaria for three years. When she was first seen, in 1927, percutaneous tests were made with a number of foods including orange, all of which gave negative results. Accordingly she was given what was then our routine diet for such cases: rice, milk and orange juice. The urticaria immediately became worse than ever before, and she left the clinic in wrath. A year later she returned, and intracutaneous tests were made which revealed a strong reaction to orange. On avoiding this and a few other foods to which she gave doubtful reactions, her attacks practically ceased, though she occasionally had a few hives from some undetermined cause.

Another instance of the occasional value of skin tests was that of a colored woman, C. C., weighing 206 pounds (93.44 Kg.), who had had generalized urticaria and angioneurotic edema of the lips, eyelids, hands and feet at intervals for twenty-four years, and migraine for about eighteen years. She knew that peaches and shrimps made her lips swell "till they nearly turned inside out," and had avoided these delicacies. Nevertheless her urticaria became more severe and troublesome. The eruption seemed to occur in frequently recurrent acute attacks rather than as a continuous chronic condition. Cutaneous tests showed doubtful reactions to potato, cocoa and tomato. Her subsequent course showed that potato was the main cause of her urticaria. By avoiding this food she remained practically free from hives for three years, though her migraine persisted.

Engman, Longcope, Rackemann and others have had similarly disappointing results with reactions to cutaneous tests in urticaria.

Substances coming in contact with the skin or inhaled were used in 1,350 intradermal and in 330 percutaneous tests. None of the latter gave positive reactions. Not even the patient with urticaria from cat hair reacted by this method. Fifty-five positive reactions to intradermal tests were obtained, thirty-five of which were in patients who also had asthma or allergic rhinitis. Only two reactions seemed of significance in regard to urticaria.

In a case of urticaria from cat hair the intracutaneous test confirmed a diagnosis suggested by the history, and in the child with a rabbit hair in the conjunctiva the diagnosis was based on the test.

Attempts to obtain reactions with extracts of the patient's urine prepared by Barber's method failed in 8 cases.

Tests with bacteria and fungi have already been mentioned. They are notoriously difficult of interpretation. Reactions to bacteria in 10 cases seemed to substantiate other evidence that the urticaria resulted from focal infection. However, such reactions, as well as those to fungi, which we have discussed, are encountered without urticaria. They entice one to make further investigation but do not yet furnish a secure basis for diagnosis.

Elimination Diets.—In many of our cases we have used a series of trial diets similar to those devised by Rowe. The results so far have been disappointing largely because food is seldom the cause of chronic urticarias.

In 49 cases in which the diets were adequately followed the outcome was as follows:

	Cases
A specific food identified as the cause of the eruption	3
Evidence of history or skin tests confirmed by dietary tests	13
Cleared while on diet, but reason for this not determined	13
Food excluded as cause of the eruptions	8
Results entirely inconclusive	12

We still consider this method worth using in obscure cases if only to exclude the influence of food.

SUMMARY

It has been our purpose in this report to separate from the mass of hypotheses that have been advanced the factors that have been demonstrated with reasonable certainty to cause urticaria. These may be listed as follows:

I. Acute urticaria (single or repeated attacks)
  A. Localized
    1. Poisons of insects, jelly-fish and plants
    2. Nontoxic substances to which the skin is sensitized
    3. Heat, cold, light and mechanical irritation

(Most agents producing generalized urticaria may also at times cause localized eruptions)

B. Generalized

4. Serum sickness and anaphylactic shock
5. Food (probably the most common cause of acute attacks)
6. Other foreign substances absorbed through the conjunctiva or the respiratory tract
7. Drugs
8. Heat (including exertion, excitement and other factors which raise the body temperature)
9. Infections
10. Menstruation

II. Chronic urticaria

11. Food (rarely the cause of chronic urticaria)
12. Focal infection (frequently the cause of chronic urticaria)
13. Animal parasites

All causes except the first group are effective only in persons with a special predisposition, which in groups 2, 4, 5, 6, 11 and 13 is clearly allergic.

The fact stands out that many cases, especially those of the severe and chronic type, could not definitely be ascribed to any of these known causes. In some cases this may be due to the difficulties of diagnosis, and in others, to the existence of multiple etiologic factors. Our experience strongly suggests, however, that some cases of urticaria must have other causes which may have long been suspected but which still await proof.

ABSTRACT OF DISCUSSION

DR. CHARLES M. WILLIAMS, New York: I am glad to hear Dr. Hopkins' support of bacterial infection as a possible cause of urticaria. I think that we see more cases of that sort as we look for them. My statement that it is more common than sensitization to food is quoted from Francis Rackemann's valuable book.

I wish to mention one case in connection with menstrual urticaria. A young woman who gave birth to a child after severe labor had marital trouble, and urticaria which continued for months developed. She was under the care of competent physicians in New York; all diets were tried, but she grew worse. She began to improve only when she received general systemic treatment and a hearty diet. Whether that indicates some deficiency of vitamin I do not know.

I agree that in the great majority of cases despite the greatest care we do not find the cause.

DR. J. FREDERICK BURGESS, Montreal, Canada: I have been rather interested in the last year in these chronic, recurrent, persistent urticarias which are extremely difficult to treat. In the last eighteen months I have seen three interesting cases, one of which I shall describe. I have been impressed with the fact that in a small percentage of these cases one is able apparently to discover an endocrine factor in the etiology.

About a year ago I saw a woman, aged 40, who had an eruption of one and a half years' duration. I had seen her a year before. At that time all the tests—metabolism, sensitization, etc.—gave negative results. I had almost exhausted the

many methods of treatment. When I again saw her, I was able to ascertain that the development of the urticaria coincided with a definite disturbance of the menstrual cycle. Also, there was a definite history of nervous and other worry, either occasioned by, or coincident with, the eruption. I gave this patient Collip's placental extract, by mouth (20 minims [1.25 cc.] three times a day, after meals). Within a short time the urticaria cleared up, and the menses became regular; she has had no recurrence. Since then I have seen two other cases which responded well to treatment.

I think that a small number of these cases are related to a break in the endocrine chain.

Dr. John H. Stokes, Philadelphia: Probably for lack of time, Dr. Hopkins made no mention of the possible psychogenous element in the background of urticaria. Especially in the protracted and resistant cases of urticaria in middle life this element may outweigh the sensitivity to a specific food and other agents, though, of course, at most it is but a factor and rarely, if ever, a sole cause. Any chronic allergic disease seems to have this shadowy neurogenous element as a background: hay fever which begins at 5:45 p. m. on August 14, year after year; asthma due to horse dander, in which the patient can by purely psychogenous methods be trained to ride behind a horse, without a wheeze; urticaria which begins the moment a stranger enters the room. Harkavy and Maisel have pointed out the way in which emotional stress influences the seizures of infectious asthma. A combination of an allergen and an emotional upset will bring on an attack of urticaria when the allergen, in subthreshold dosage, so to speak, has not produced an outbreak since desensitization was accomplished. The psychogenous factor may enter even into the field of the physical allergies. I have occasion to describe urticaria to some patients as "cutaneous tears," so insistently in the life of the person does it limit its activity to periods of nervous stress. Note that I am not proposing psychogenous factors as sole causes. They work through a physical mechanism, such as the vasomotor system or the gastro-intestinal tract. By a correction of the psychogenous warp it is possible—and sometimes only thus possible—to procure lasting amelioration of a persistent "urticariogenic" state.

Dr. Howard J. Parkhurst, Toledo, Ohio: Speaking of inhalants, it might be interesting to mention that Dr. K. D. Figley and I have found five patients in Toledo with more or less generalized chronic eczema and recurrent outbreaks of papular urticaria, who were sensitized to silk dust as an inhalant and not as a contact substance. We succeeded in completely desensitizing one of these patients by injections of silk extract.

Dr. Samuel Ayres, Jr., Los Angeles: I was glad to see reference to urticaria caused by animal parasites. When speaking of this type one usually thinks of fleas, mosquitoes and insects of that sort, but I have seen three cases in the last few years which were quite illuminating. One was a typical case of urticaria due to scabies. The patient was for several months in the hands of an allergist who had made many cutaneous tests without avail. The patient was married to a physician, and every night she required epinephrine before being able to sleep. As she was a very clean person and bathed frequently, only few scabetic lesions were present, but one typical burrow was discovered from which an acarus was extracted. Three applications of an antiparasitic ointment cured the urticaria.

In the last few weeks I have also seen a case of generalized pediculosis pubis on a very hairy man who was allergic to the parasites. On the chest he had a patch that appeared as if a mustard plaster had been applied, and numerous wheals were scattered over the body. Following eradication of the pediculosis the urticaria was relieved.

In another case, a child was relieved of urticaria when pediculosis of the scalp cleared up. In another instance of urticaria due to bacteria or fungi a case of seborrheic dermatitis of the scalp of ten years' duration was accompanied by urticaria of equal duration. The urticaria cleared up within ten days following applications to the scalp of an ointment containing sulphur and a salicylic preparation. With carelessness in the care of the scalp the urticaria reappeared, but following a second application it again cleared up.

Dr. J. G. Hopkins, New York: I am glad that Dr. Williams agreed with me on bacterial urticaria.

I am also grateful to Dr. Stokes for mentioning the question of psychic urticaria. There was no case in which we could prove that a psychic stimulus was the sole cause of the urticaria, though in one this seemed probable. There seems to be little doubt that psychic stress may aggravate the symptoms, and there is much to suggest that it may release a reaction prepared by other causes.

Török made an illuminating comment on Duke's cases of heat urticaria. You will recall that he described two types, one in which the local application of heat caused a localized urticaria, and another in which anything which raised the temperature of the body caused a generalized outbreak. In one patient of the second type a fit of anger raised the body temperature, and this was followed by an urticarial attack. Török suggested that this may be the explanation of many supposedly psychic cases. We had two cases of the second type. The application of hot water to the skin caused no hives, but exercise while the patient was wrapped in blankets brought on a typical attack. One of these patients became nervous while waiting to be examined, and although he had had no hives for several weeks, he came in with a large number of them. I do not believe that this was psychic urticaria but rather heat urticaria caused by elevation of the temperature of the body under excitement. Such cases make one hesitate to accept psychic stimuli as the basic cause of urticarias.

ACUTE INTERSTITIAL MYOCARDITIS

REPORT OF A CASE FOLLOWING A SEVERE DERMATITIS DUE TO SULPHUR OINTMENT

ELMER S. MAXWELL, M.D.
AND
CAREY C. BARRETT, M.D.
LEXINGTON, KY.

Fiedler, in 1889, described an uncommon type of myocarditis, which he designated as acute interstitial myocarditis. There have been reported in the continental literature thirty-six cases with postmortem studies. In this country, Scott and Saphir [1] were the first to call attention to this disease. They reported two cases of their own, and later cases were reported by Bailey and Andersen,[2] de la Chapelle and Graef [3] and Maslow and Lederer.[4]

The condition has been variously designated as "interstitial," "circumscribed," "diffuse," "isolated," "idiopathic" and "primary" myocarditis.

The clinical picture is one of progressive myocardial failure, with or without pain in the chest, usually following some widespread infection. Bailey and Anderson point out that:

> In a large number of the reported cases the myocardial failure started during or shortly after an acute infection. In one of Kaufmann's cases the patient had an infected burn, and the other, an infection of the operative wound following the removal of tuberculous cervical lymph nodes. One of Saltykow's cases had a healing burn, the other an incision for drainage of an abscess of the jaw ten days prior to the onset of the heart symptoms. One of Sellentin's patients had a carbuncle of the neck opened four weeks previously. Wolf's patient had an abrasion of the arm. Zuppinger reports a case in which an infection of the foot was incised thirteen days before the onset of the cardiac symptoms. His other patient had a skin infection of the left groin. One of Fiedler's patients had been troubled for some time with leg ulcers; the other had previously had a hemorrhagic skin eruption.

---

1. Scott, R. W., and Saphir, O.: Acute Isolated Myocarditis, Am. Heart J. **5**:129 (Dec.) 1929.

2. Bailey, F. R., and Andersen, D. H.: Acute Interstitial Myocarditis, Am. Heart J. **6**:338 (Feb.) 1931.

3. de la Chapelle, C. E., and Graef, I.: Acute Isolated Myocarditis, with Report of a Case, Arch. Int. Med. **47**:942 (June) 1931.

4. Maslow, H. L., and Lederer, M.: Interstitial Myocarditis in a Child Nineteen Months of Age, Am. J. Dis. Child. **45**:807 (April) 1933.

They conclude that although there is no known etiology, the frequent association of the disease with infections, especially with pyogenic infections of the skin, is suggestive. In the case reported by Maslow and Lederer the patient had a purulent conjunctivitis and a severe stomatitis and pharyngitis of unknown etiology.

The heart usually shows some hypertrophy which is rarely marked. The musculature is frequently described as flabby, although in some cases it is firm. There is no involvement of the heart valves. The surface of the cut section frequently shows small grayish flecks or streaks. The changes are usually limited to the wall of the left ventricle, although occasional lesions are found in the auricles and in the right ventricle. Mural thrombi are a common finding. Outside of the heart there are no gross or microscopic pathologic changes of any importance, except those of a toxic nature in the abdominal organs.

Histologically the picture is remarkably constant: An interstitial cellular infiltration consisting of lymphocytes, polymorphonuclears, plasma cells, fibroblasts, eosinophils and wandering cells in varying combinations is the characteristic lesion. The cardiac muscle cells show varying degrees of degeneration, some a complete necrosis, and, in older lesions, replacement by connective tissue. The cellular infiltration is in the perivascular connective tissue and between the muscle cells. Edema sometimes causes a further separation of the muscle cells. Some authors describe a parenchymatous cellular deposit. Frequently the inflammatory lesion extends to and involves the endocardium.

The following case is reported as another example of acute interstitial myocarditis:

REPORT OF A CASE

History.—E. S., a white man, a dentist, aged 53, was first seen by one of us (C. C. B.) on Feb. 9, 1932, complaining of a generalized pruritic eruption. The onset of his present illness was in November, 1931, at which time he had some pain in the left side of the chest. He strapped his chest with adhesive tape, and when this was removed, the skin was found to be inflamed and pruritic. The eruption was treated with various home remedies, and it gradually spread to other parts of the body. On Jan. 21, 1932, a diagnosis of scabies was made by his family physician, and a proprietary sulphur ointment, of the type described by Oellers, was prescribed. The patient applied this once a day for six successive days to his entire body, including the face. The condition became much worse.

Physical Examination.—The patient was a well developed and well nourished man who appeared somewhat older than his stated age. He was obviously very uncomfortable. His entire skin was brownish red; there were some scaling but no exudation, much edema of the legs, and many small tense blebs. His temperature was 100.5 F. The other findings of the physical examination were essentially negative. The heart was normal to palpation and percussion. The heart sounds were normal. The examination of the lungs gave negative results except for a small area of dulness and distant breath sounds over the lower lobe of the left lung posteriorly. There were no palpable masses or tenderness in the abdomen.

Examination of the urine showed: reaction, acid; specific gravity, 1.1018; no albumin, sugar, blood, casts or pus. Examination of the blood revealed: red blood cells, 4,340,000; hemoglobin, 74 per cent; white blood cells, 15,700. The differential count showed 92 per cent polymorphonuclears.

Course.—The patient was treated with colloidal tub baths and with various soothing remedies. His course was stormy. A great number of blebs developed which were at first filled with clear fluid and later became purulent; still later they changed to thick yellow crusts that covered raw denuded areas. The patient had a septic type of temperature with daily variations from normal to 103 F. A blood culture taken on Feb. 26, 1932, was positive for Staphylococcus haemolyticus. This was thought to be due to contamination, because it was impossible to cleanse the patient's skin properly. About March 3, a very severe inflammation developed in the nasal passages, the pharynx, and the larynx. A culture taken from the nose and throat was positive for Staphylococcus haemolyticus. At this time the patient first complained of a slight dyspnea, which in a few days became quite marked.

His condition gradually improved so that by March 18 the pharyngitis and laryngitis had disappeared; the temperature was normal, and the dermatitis was much improved. He had, however, a little dyspnea and a little pitting edema of the ankles. On examination the urine showed: albumin, 2+; pus, 1+; hyaline cast, 1+.

The temperature remained normal for a few days, and then there were daily gradual rises to a maximum of 101 F. The dyspnea gradually grew worse. On April 8 he had a severe attack of dyspnea. He became cyanotic, pulseless and extremely dyspneic. He recovered from this attack in about two hours. The next morning he was obviously much weaker. The pulse had a gallop rhythm. For the first time there was some edema of the scrotum. The ankles showed considerable edema. He had another attack of dyspnea on that day and died within a few minutes.

At no time did he have any anginal pains. During the last three weeks of his illness he complained a little of a slight dull pain in the region of the left kidney. There was never any palpable mass or tenderness of this area.

Autopsy (E. S. M.).—The body was that of a well developed and well nourished white man aged about 53. The skin was mottled by numerous areas of increased pigmentation, and many small blebs were scattered over the trunk and extremities. A slight diffuse edema was apparent. The scrotum was markedly edematous. Each pleural cavity contained about 600 cc. of clear amber-colored fluid. The lungs were moderately edematous. The lower lobe of the left lung showed some atelectasis. The pericardial cavity contained about 50 cc. of clear fluid. The pericardium and epicardium showed no abnormalities.

The heart was moderately enlarged, weighing 545 Gm. The wall of the left ventricle was thickened, and on section showed a number of small grayish areas. The endocardium showed no gross lesions. The mitral cusps were definitely thickened but were apparently competent. The aortic cusps were smooth, slightly thickened and slightly fenestrated. The right side of the heart presented no unusual features. The opening of the left coronary artery was slightly narrowed; that of the right was almost completely obliterated. The descending branch of the left coronary artery showed marked sclerosis with considerable calcification and moderate narrowing of the lumen. No thrombus could be demonstrated in this vessel. The transverse branch showed these changes to a lesser degree. The

right artery presented only slight sclerosis. The first portion of the aorta showed extensive atherosis.

The liver was somewhat enlarged, but the surface was smooth. The gallbladder and ducts were apparently normal. The spleen, suprarenal glands and pancreas were grossly normal. The kidneys were enlarged, measuring 14 cm. in length with a number of small petechiae apparent beneath the capsule. The capsule stripped with slight resistance, revealing a finely granular surface. The kidneys, on section, revealed a normal architecture.

The gastro-intestinal tract and the pelvic organs showed no abnormalities. The retroperitoneal tissues were edematous.

Histopathologic Examination.—Sections from the skin showed lymphoid infiltration but no changes suggesting the cause of the lesion.

Section of heart muscle showing the characteristic interstitial deposit.

Sections from the wall of the left ventricle showed, for the most part, only cloudy swelling and slight fatty changes in some of the muscle cells. However, certain areas showed a marked interstitial polymorphonuclear infiltration. A moderate number of lymphocytes and a few eosinophils were also present. Where the cellular infiltration was most marked, the muscle cells were separated by edema. Definite degenerative changes were present in some of the muscle cells, while some showed marked hypertrophy. Where the inflammatory lesion extended to the endocardium this membrane also showed a cellular infiltration. No bacteria could be found in Gram stains. No thrombosis could be demonstrated in the smaller arterioles. No inflammation was found in the auricles or in the right ventricular wall.

The kidneys showed marked degeneration in the epithelium of the convoluted tubules. Some glomeruli presented active inflammation, and a moderate number were sclerotic. The liver showed albuminous degeneration and moderate passive congestion.

Anatomic Diagnosis.—The diagnosis was: acute interstitial myocarditis; cardiac hypertrophy; coronary sclerosis; aortic atherosis; bilateral pleural effusion;

chronic dermatitis; subacute glomerular nephritis; generalized edema, and granular degeneration of the parenchymatous tissues.

COMMENT

Several authors have noted that acute interstitial myocarditis frequently follows a pyogenic infection of the skin. The patient whose case is reported had a most extensive infection of the skin and mucous membranes with Staphylococcus haemolyticus. Postmortem examination did not show any evidence of septicemia so that if the myocarditis was related to the pyogenic infection, it must have been through the absorption of bacterial toxins. The gross and microscopic appearance of the abdominal viscera supported this view.

No case of acute interstitial myocarditis has ever been diagnosed before death. However, with the picture of progressive myocardiac failure following a pyogenic infection of the skin and without septicemia, the cardiac lesion could have been reasonably suspected.

It seems timely to emphasize the disastrous results that may follow the indiscriminate use of proprietary remedies.

SARCOID OF BOECK

LESTER HOLLANDER, M.D.
AND
CLARA R. SCHLESINGER, B.A.
PITTSBURGH

The controversy as to the etiology of Boeck's sarcoid has been raging since the time it was first described by Boeck in 1897. And although the opinions on this subject are still varied, they seem to be overwhelmingly in favor of the hypothesis that sarcoid is the product of a reaction caused by the tubercle bacillus.

Recently Kissmeyer,[1] in an excellent monograph on this subject, reviewed Boeck's original contention that sarcoid is a disease *sui generis*. Kissmeyer classified it as a specific, chronic granulomatous process, one which stands midway between tuberculosis and leprosy. He based this opinion on five points: (1) the absence of a positive tuberculin reaction; (2) the infrequency with which tubercle bacilli have been demonstrated in sarcoid; (3) the peculiar swelling in the hilar glands in the mediastinum; (4) the occurrence of osseous changes in the phalanges of the fingers and toes, giving rise to a rarefaction of bone structure and to the formation of cystic changes, which he called osteitis multiplex cystica, and (5) the almost specific therapeutic effect of solution of potassium arsenite on the disease.

Each of these points is controversial, and has not been accepted. Martenstein[2] explained the absence of a tuberculin reaction on the basis of anergy. Kyrle[3] demonstrated that the tubercle bacilli can be found if early lesions are examined. This was confirmed by Schaumann, Reute, Martenstein, Dietrich and others. The swelling of the hilar glands is a frequent observation in tuberculosis of the lymph glands. Kohler,[4] in his recent book on roentgenology, considered the bony

From the Pittsburgh Skin and Cancer Foundation.

Excerpts from a paper read before the Section on Dermatology of the Medical Society of the State of Pennsylvania, Pittsburgh, Oct. 5, 1932.

1. Kissmeyer, A.: La maladie de Boeck, Copenhagen, Levin and Munksgaard, 1932.

2. Martenstein: Sarkoid Boeck und Lupus Pernio, Arch. f. Dermat. u. Syph. **147**:70, 1924.

3. Kyrle, Joseph: Die Anfangsstadien d. Boeckshen Lupoids, Arch. f. Dermat. u. Syph. **131**:33, 1931.

4. Kohler, Alban: Roentgenology, New York, William Wood & Company, 1928, p. 19.

changes tuberculous and named the process osteitis tuberculosa multiplex cystica. And Kissmeyer's fifth point, that solution of potassium arsenite is a specific, is greatly doubted, as evidenced by the expression of Darier.[5]

Evidence has been mounting to the effect that sarcoid of Boeck is only a special form of tuberculosis, and the study submitted seems to further the substantiation of this contention.

The studies of the blood pictures in four cases are submitted, including two cases of sarcoid of Boeck, one case of tuberculosis of the hypoderm of Wende and one case of lupus pernio (?) or sarcoid, all showing a definite leukocytic response, similar in certain respects.

REPORT OF CASES

CASE 1.—*Sarcoid of Boeck.*—Mrs. S. M., Slavish housewife, 39 years old, was first examined on Feb. 5, 1931, on account of an eruption of seven years' duration affecting her face, hands and feet. Three rounded, deeply infiltrated, flesh-colored lesions, having a definite brownish tinge, were found on the face—one at the upper orbital region, one on the cheek and one on the tip of the nose. They were traversed by a number of telangiectasias; diascopic pressure intensified the brownish color.

The distal phalanges of all the fingers and toes, the middle phalanges of the first, third and fifth finger of the left hand and the middle phalanx of the fifth finger of the right hand were widened, enlarged and flattened, giving the fingers and toes a cat-o'-nine-tails appearance. The skin over these phalanges was atrophic and reddish brown and was traversed by a number of telangiectasias. Roentgen examination showed a spongy character of the bones and the presence of osteitis tuberculosa multiplex cystica.

Another positive finding was the presence of diffuse infiltration in both pulmonic fields. This was limited to the hilus and the median zones. The basal metabolic rate on three different occasions was +51.3, +39.4 and +41.6. A specimen taken from one of the fingers for biopsy showed a typical example of sarcoid of Boeck.

After about six months of therapeutic use of tuberculin, the tuberculin reaction, which at first was entirely negative, became strongly positive, and treatment with tuberculin had to be discontinued. The lesions on the face involuted, but those on the extremities remained unaltered.

The study of the blood picture was carried out for thirty months at about weekly intervals. Analysis of this study shows the red blood cells, hemoglobin and color index within normal limits. The total number of leukocytes, with an exceptional high and low peak, is also a low normal one. The differential count, however, shows a different condition. The polymorphonuclear neutrophils maintained an average level slightly below normal, with an occasional temporary peak-like elevation. The lymphocytes, on the other hand, were consistently much below normal, whereas the monocytes remained normal, so that the lymphocytes and monocytes frequently approximated each other. This blood picture is not unusual in tuberculosis.

5. Darier, quoted by Kissmeyer.[1]

CASE 2.—*Sarcoid of Boeck.*—Mrs. B. L., an American housewife, aged 37, was first examined on Aug. 4, 1930, on account of small, yellowish-brown lesions varying from the size of a pin to that of a split pea, which appeared on the lower

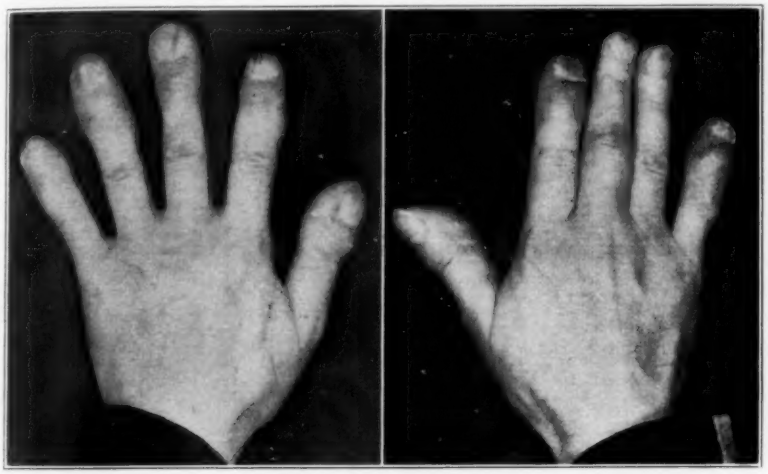


Fig. 1 (case 1).—Sarcoid of Boeck, showing the cat-o'-nine-tails appearance.

Fig. 2 (case 2).—Sarcoid of Boeck (miliary lupoid), showing the pin-point lesions.

portion of the face on both sides. The eruption, which was rapid in its onset, consisted of several hundred lesions and was of one month's duration. Diascopic pressure revealed fine brownish nodules under the glass.

TABLE 1.—*Study of Blood Picture (Case 1)*

Date	Red Cells	Hemoglobin, per Cent (Sahli)	Color Index	White Cells	Polymorphonuclears, per Cent	Lymphocytes, per Cent	Monocytes, per Cent
2/ 5/31	4,620,000	73	0.80	5,400	80.0	15.0	5.0
2/25/31	3,920,000	71	0.90	4,600	66.5	22.0	10.0
3/ 2/31	4,220,000	61	0.72	8,000	76.5	17.5	4.5
3/11/31	4,020,000	66	0.82	2,800	76.0	16.0	7.5
3/20/31	4,250,000	63	0.75	4,800	68.0	24.0	5.5
3/25/31	3,210,000	62	0.96	2,800	72.0	18.0	9.0
3/30/31	4,130,000	64	0.78	2,400	78.0	15.0	5.5
4/ 8/31	4,630,000	71	0.77	8,400	76.6	14.3	7.1
4/15/31	4,350,000	65	0.75	7,200	67.0	26.5	6.0
4/22/31	4,500,000	62	0.68	7.200	67.0	23.0	9.0
4/29/31	4,040,000	56	0.70	8,600	72.0	22.0	5.5
5/ 6/31	3,670,000	62	0.85	5,200	73.3	17.3	7.3
5/13/31	4,290,000	62	0.73	6,400	80.0	12.0	7.0
5/20/31	3,750,000	59	0.79	4,800	78.0	9.0	12.0
5/27/31	3,900,000	55	0.70	6,400	70.5	18.2	5.2
6/ 3/31	3,950,000	59	0.75	5,400	70.5	14.0	11.0
6/10/31	4,080,000	58	0.71	5,000	72.0	22.0	5.0
6/17/31	3,820,000	63	0.83	5,000	68.0	25.0	6.0
6/24/31	3,770,000	64	0.85	6,800	81.5	12.0	2.5
7/ 1/31	4,330,000	69	0.80	7,800	82.0	14.0	3.5
7/ 8/31	4,470,000	73	0.82	6,000	72.0	19.5	8.0
7/15/31	4,160,000	71	0.85	6,800	73.0	20.5	4.5
7/29/31	4,400,000	72	0.81	5,600	72.5	21.0	4.5
8/ 5/31	4,620,000	73	0.79	4,000	73.0	18.0	5.0
8/12/31	4,190,000	74	0.89	4,800	68.0	19.5	10.0
8/19/31	4,510,000	71	0.79	4,000	79.5	11.5	6.5
8/26/31	4,310,000	64	0.74	5,400	74.0	13.5	9.0
9/ 2/31	4,370,000	67	0.77	4,600	71.5	17.5	8.5
9/10/31	4,070,000	64	0.79	8,600	71.5	21.5	6.0
9/17/31	4,370,000	73	0.83	5,000	63.5	27.0	7.5
9/24/31	3,730,000	71	0.96	4,800	67.5	22.0	10.0
10/ 1/31	3,770,000	74	1.00	4,600	75.0	10.0	13.0
10/ 8/31	4,620,000	74	0.80	3,200	67.0	23.0	7.0
10/15/31	4,610,000	67	0.73	6,000	56.0	37.0	6.0
10/22/31	3,960,000	71	0.90	7,400	74.5	14.5	8.0
10/29/31	4,540,000	68	0.75	3,000	78.5	15.0	5.0
11/ 5/31	4,410,000	68	0.77	4,000	63.0	21.5	11.0
11/12/31	4,490,000	65	0.73	7,400	66.0	20.0	9.0
11/19/31	4,470,000	67	0.75	8,000	75.0	17.0	5.0
12/ 3/31	3,750,000	60	0.80	6,400	73.0	14.0	11.0
12/10/31	4,150,000	64	0.78	5,800	66.4	20.4	8.0
12/17/31	4,130,000	61	0.74	8,000	66.8	21.2	10.0
12/24/31	4,180,000	61	0.74	8,800	74.7	16.0	6.0
12/31/31	3,870,000	59	0.76	5,400	65.5	24.5	6.7
1/ 7/32	4,010,000	61	0.76	5,000	66.2	28.0	4.2
1/21/32	4,470,000	71	0.78	4,200	67.6	19.6	10.6
1/28/32	3,520,000	59	0.84	4,600	75.6	16.0	7.6
2/ 4/32	4,690,000	66	0.81	11,600	76.8	15.6	6.0
2/11/32	4,320,000	65	0.75	4,600	73.0	19.2	4.7
2/18/32	4,170,000	63	0.76	4,600	69.0	17.0	12.2
2/25/32	4,500,000	64	0.71	6,800	60.3	22.6	8.3
3/ 3/32	4,420,000	66	0.75	4,200	72.0	13.6	9.2
3/17/32	4,290,000	57	0.67	4,600	75.3	17.3	6.0
3/24/32	4,100,000	58	0.70	6,000	69.2	17.2	9.8
3/31/32	3,870,000	57	0.74	5,000	76.0	17.0	6.4
4/ 7/32	4,270,000	64	0.75	6,600	76.8	15.4	5.8
4/14/32	4,850,000	68	0.71	8,600	68.1	18.8	6.8
4/21/32	4,720,000	65	0.69	10,400	75.8	18.9	4.9
5/12/32	3,950,000	59	0.76	6,600	72.8	20.6	6.0
5/19/32	3,750,000	51	0.69	4,200	65.4	22.4	6.2
5/26/32	4,130,000	58	0.71	5,400	64.2	30.0	4.2
6/16/32	4,260,000	60	0.77	4,000	64.8	27.6	5.2
6/24/32	4,690,000	68	0.74	6,200	70.8	16.8	6.4
7/ 5/32	4,120,000	66	0.80	6,800	64.6	20.6	9.8
7/12/32	4,030,000	57	0.71	4,400	73.6	16.6	6.3
7/22/32	4,410,000	57	0.65	7,600	68.6	20.6	4.8
8/23/32	4,120,000	67	0.82	7,200	53.2	26.4	16.0
8/26/32	4,820,000	65	0.68	10,800	74.4	17.6	6.0
9/ 9/32	4,490,000	68	0.76	5,400	63.2	28.4	5.2
10/ 7/32	4,200,000	66	0.78	4,000	62.6	19.4	13.4
10/20/32	3,870,000	61	0.79	7,200	57.2	32.8	8.0
11/ 3/32	4,130,000	56	0.68	6,200	65.3	24.0	6.6
11/17/32	4,580,000	67	0.73	9,200	70.8	17.2	11.2
12/ 1/32	4,550,000	71	0.79	6,400	75.2	16.8	5.6
12/15/32	4,610,000	66	0.72	7,200	76.4	13.6	9.2
12/29/32	4,370,000	64	0.73	6,200	71.4	16.6	8.0
1/12/33	4,470,000	71	0.80	4,800	72.4	16.8	8.0

TABLE 1.—*Study of Blood Picture (Case 1)—Continued*

Date	Red Cells	Hemoglobin, per Cent (Sahli)	Color Index	White Cells	Polymorphonuclears, per Cent	Lymphocytes, per Cent	Monocytes, per Cent
1/26/33	4,380,000	62	0.71	7,800	74.0	13.2	9.6
2/ 9/33	4,130,000	59	0.72	5,800	76.4	15.2	7.2
2/23/33	4,270,000	68	0.80	8,800	78.8	14.4	4.8
3/ 9/33	4,690,000	71	0.76	7,400	74.0	17.6	6.4
3/23/33	4,210,000	66	0.79	5,400	71.0	18.5	7.0
3/29/33	4,430,000	66	0.75	5,600	76.0	19.2	4.5
4/20/33	4,350,000	67	0.75	2,400	73.6	12.8	9.6
5/ 4/33	4,420,000	62	0.70	3,600	64.0	24.0	10.4
5/18/33	3,730,000	52	0.70	5,800	77.6	15.2	6.4
6/ 1/33	4,010,000	58	0.71	5,000	60.8	28.8	8.4
6/ 8/33	4,570,000	66	0.72	1,800	73.6	15.2	8.0
6/15/33	4,670,000	67	0.72	4,400	65.6	28.4	5.6
6/26/33	4,470,000	73	0.82	4,000	78.4	15.2	4.8
7/ 6/33	4,310,000	63	0.73	6,000	77.6	15.2	4.8
7/13/33	4,190,000	64	0.77	3,400	74.4	18.0	6.0
7/27/33	3,790,000	65	0.88	4,900	73.6	21.6	3.2
8/10/33	4,420,000	65	0.74	5,400	72.8	19.2	4.8
8/31/33	3,930,000	63	0.83	4,400	61.6	27.2	6.8

TABLE 2.—*Study of Blood Picture (Case 2)*

Date	Red Cells	Hemoglobin, per Cent (Sahli)	Color Index	White Cells	Polymorphonuclears, per Cent	Lymphocytes, per Cent	Monocytes, per Cent
8/ 4/30	4,710,000	78	0.83	6,000	59.5	37.5	1.5
9/25/30	4,540,000	78	0.86	4,800	66.0	29.0	3.5
10/ 9/30	4,520,000	75	0.83	5,400	65.5	30.5	3.0
10/16/30	4,430,000	73	0.83	7,800	50.5	43.5	2.5
10/23/30	4,250,000	75	0.90	9,600	67.5	26.0	2.5
11/13/30	4,140,000	73	0.90	7,200	63.5	27.5	4.0
11/20/30	4,050,000	74	0.80	8,200	63.0	26.0	8.0
11/26/30	4,010,000	74	0.90	5,600	59.5	30.5	7.0
12/ 4/30	3,870,000	70	0.90	5,400	64.5	25.0	6.5
12/11/30	3,830,000	72	0.94	6,600	69.5	22.0	6.0
12/18/30	3,730,000	72	0.97	5,200	60.0	31.0	4.0
12/24/30	3,960,000	71	0.89	7,200	57.5	29.5	8.0
12/31/30	3,800,000	66	0.87	6,600	63.5	22.0	9.0
1/ 8/31	4,010,000	68	0.85	7,000	61.6	26.8	8.8
1/15/31	4,230,000	65	0.77	9,200	75.5	19.0	3.5
1/22/31	4,220,000	67	0.80	8,200	68.5	23.5	5.0
1/29/31	4,300,000	72	0.80	6,800	72.6	17.3	8.3
2/ 5/31	4,020,000	67	0.83	7,400	62.5	28.5	8.0
2/26/31	4,500,000	81	0.90	13,400	77.0	17.5	4.5
3/ 5/31	4,500,000	79	0.87	6,800	64.0	29.0	4.0
3/12/31	4,350,000	74	0.86	6,600	62.0	28.0	8.0
3/26/31	4,150,000	73	0.90	8,800	65.0	27.0	5.5
4/ 2/31	3,840,000	67	0.88	9,800	68.0	24.0	6.0
4/ 9/31	4,410,000	69	0.80	6,200	64.0	25.0	7.5
4/16/31	3,840,000	71	0.90	9,800	61.0	32.0	5.5
4/30/31	3,820,000	65	0.85	8,400	66.5	28.0	2.0
5/21/31	4,150,000	64	0.78	7,800	67.0	32.0	1.0
6/ 4/31	4,320,000	66	0.77	9,000	72.5	23.0	4.0
6/18/31	3,870,000	65	0.84	6,600	73.0	24.5	2.0
7/ 2/31	4,190,000	73	0.89	4,000	61.5	28.0	7.5
7/16/31	4,500,000	74	0.82	5,000	66.5	27.0	4.0
7/30/31	4,420,000	78	0.88	8,200	72.0	25.0	1.5
8/13/31	4,470,000	72	0.80	5,200	63.0	29.5	3.0
8/27/31	4,520,000	76	0.84	7,600	73.0	21.5	3.5
9/10/31	4,460,000	77	0.86	6,200	61.6	31.0	3.3
9/24/31	4,420,000	74	0.84	5,200	65.5	27.0	6.5
10/ 8/31	4,340,000	76	0.88	5,000	47.0	49.0	1.0
10/22/31	3,860,000	70	0.91	8,400	68.0	27.0	2.5
12/ 3/31	4,360,000	67	0.77	6,600	66.5	27.0	3.5
12/17/31	4,020,000	61	0.76	8,000	66.5	25.5	4.5
1/ 8/32	4,370,000	74	0.85	6,000	58.5	36.5	2.5
1/14/32	4,140,000	76	0.92	5,800	59.5	34.5	3.0
1/28/32	4,070,000	75	0.92	5,200	65.6	29.2	4.4
2/12/32	4,410,000	74	0.84	7,400	69.6	24.8	3.2
3/30/32	4,280,000	74	0.87	7,800	67.8	27.0	4.8
4/ 7/32	4,070,000	74	0.91	6,600	61.2	32.4	3.6
6/ 9/32	4,150,000	69	0.84	6,200	74.4	21.2	2.4
6/21/32	4,360,000	68	0.78	5,600	64.0	30.2	2.4

Fig. 3 (case 3).—Tuberculosis of the hypoderm (Wende).

Fig. 4 (case 3).—Multiple lesions on the body.

TABLE 3.—*Study of Blood Picture (Case 3)*

Date	Red Cells	Hemoglobin, per Cent (Sahli)	Color Index	White Cells	Polymorphonuclears, per Cent	Lymphocytes, per Cent	Monocytes, per Cent
12/10/30	4,450,000	66	0.75	6,600	66.0	26.0	5.0
12/22/30	4,150,000	67	0.81	7,600	63.0	26.0	6.0
12/26/30	4,230,000	64	0.76	6,600	57.0	31.0	10.0
12/31/30	4,210,000	65	0.77	3,600	67.5	21.5	9.0
1/ 5/31	3,820,000	65	0.85	6,200	59.0	32.0	8.0
1/10/31	4,230,000	66	0.78	4,000	68.0	19.0	9.0
1/16/31	4,050,000	60	0.73	5,400	56.0	26.0	15.3
1/21/31	4,210,000	62	0.73	5,600	66.0	25.0	7.0
1/26/31	4,460,000	62	0.70	6,400	54.0	34.0	10.0
2/ 2/31	4,410,000	68	0.77	4,800	58.6	30.6	9.3
2/ 9/31	4,230,000	64	0.76	2,000	53.0	36.0	10.0
2/14/31	3,900,000	60	0.77	13,600	61.0	25.0	11.0
2/19/31	4,260,000	62	0.73	3,600	61.0	29.0	9.0
2/25/31	3,870,000	60	0.78	3,400	66.0	24.0	8.0
3/ 2/31	4,130,000	59	0.71	1,800	76.0	18.0	6.0
3/ 6/31	4,020,000	63	0.78	2,600	60.0	29.5	8.5
3/25/31	4,340,000	66	0.76	4,000	68.0	24.0	7.0
4/ 6/31	4,610,000	74	0.80	4,400	57.0	30.0	9.0
4/13/31	3,810,000	65	0.85	2,200	66.0	26.0	4.0
4/20/31	4,350,000	63	0.73	2,600	55.0	36.0	6.0
5/ 4/31	3,630,000	58	0.80	3,600	59.0	27.0	9.0
5/11/31	3,850,000	64	0.84	3,000	62.0	19.0	16.0
5/29/31	4,120,000	60	0.73	1,800	74.0	17.0	9.0
6/ 4/31	4,050,000	56	0.70	1,200	58.6	32.0	8.0
6/11/31	4,470,000	73	0.82	4,000	53.0	33.0	8.0
6/18/31	4,200,000	69	0.72	3,000	63.5	30.0	4.5
6/25/31	4,230,000	67	0.80	4,000	68.0	24.0	7.0
7/ 2/31	4,540,000	74	0.82	3,200	69.5	23.5	4.5
7/ 9/31	4,330,000	73	0.84	4,200	58.5	31.0	8.0
7/17/31	4,430,000	72	0.81	5,000	68.0	25.0	4.0
7/24/31	4,310,000	72	0.83	3,000	58.5	34.5	6.5
7/31/31	4,240,000	71	0.84	5,600	70.0	19.0	8.0
8/11/31	3,920,000	67	0.86	3,000	62.5	28.0	7.5
8/18/31	4,660,000	77	0.83	3,200	57.3	34.0	6.6
8/25/31	4,420,000	76	0.86	2,600	61.0	31.0	6.6
9/ 2/31	4,210,000	72	0.85	3,800	63.0	31.0	4.0
9/ 9/31	4,360,000	73	0.84	4,000	54.0	38.0	5.0
9/16/31	4,160,000	71	0.85	3,200	65.0	27.0	5.0
9/23/31	4,220,000	72	0.85	2,000	67.0	22.3	9.3
9/30/31	3,850,000	64	0.84	4,800	64.5	28.0	7.0
10/ 7/31	4,110,000	60	0.73	3,400	59.5	30.0	6.5
10/21/31	4,500,000	67	0.73	3,600	55.0	33.0	10.5
10/29/31	4,050,000	66	0.82	3,400	63.0	28.0	9.0
11/ 9/31	3,750,000	62	0.83	5,800	67.0	24.0	7.5
11/16/31	4,350,000	68	0.79	5,800	72.5	21.5	3.5
11/23/31	4,200,000	61	0.72	3,600	63.5	28.0	8.0
11/30/31	4,240,000	64	0.76	5,000	64.0	30.6	3.3
12/ 7/31	4,290,000	61	0.72	4,200	58.5	31.5	9.0
12/14/31	4,160,000	64	0.77	3,400	57.2	34.0	6.0
12/28/31	4,390,000	69	0.79	3,800	60.0	34.5	4.5
1/25/32	4,270,000	69	0.81	4,200	67.0	24.0	6.0
1/11/32	4,390,000	71	0.81	4,400	58.0	29.3	12.0
2/ 8/32	4,120,000	66	0.80	4,600	59.2	32.4	6.8
2/25/32	4,220,000	64	0.78	5,000	59.0	30.2	8.8
3/15/32	3,970,000	65	0.82	4,600	68.6	24.8	6.2
3/22/32	3,770,000	57	0.76	2,600	67.6	23.6	7.2
3/31/32	3,760,000	57	0.76	2,600	63.0	30.6	5.6
4/18/32	4,090,000	74	0.91	2,400	64.0	24.0	10.0
5/24/32	4,150,000	64	0.78	2,200	70.4	24.8	3.2
6/ 8/32	4,220,000	61	0.72	4,600	64.8	31.6	2.8
7/ 5/32	4,370,000	64	0.73	2,400	70.8	22.4	3.6
8/ 9/32	4,220,000	66	0.78	3,900	63.4	31.6	4.0
8/10/32	4,790,000	71	0.75	4,000	66.0	30.0	3.0
8/12/32	4,890,000	78	0.80	7,750	71.6	22.0	4.8
8/13/32	4,870,000	70	0.72	5,200	56.8	33.6	6.4
8/15/32	4,730,000	70	0.74	4,970	67.2	30.4	1.6
8/16/32	4,690,000	72	0.77	6,820	63.2	32.8	2.4
8/17/32	4,770,000	74	0.78	6,600	72.4	22.0	4.0
8/18/32	4,720,000	73	0.78	5,600	68.0	28.0	2.4
8/22/32	4,730,000	76	0.81	3,250	62.4	29.6	5.6
8/24/32	4,590,000	66	0.74	3,250	66.5	29.0	3.5
8/25/32	4,500,000	64	0.71	3,770	61.5	33.7	3.2
8/26/32	4,360,000	65	0.75	3,400	66.4	28.8	4.4
8/27/32	4,430,000	65	0.74	3,420	62.0	29.2	5.6
8/30/32	4,710,000	69	0.73	6,800	66.0	27.8	3.8
9/ 1/32	4,610,000	77	0.83	4,400	60.8	32.8	4.0
9/22/32	4,720,000	84	0.89	3,400	63.6	30.8	3.2
9/29/32	4,430,000	72	0.82	4,600	54.0	40.8	3.2
10/ 6/32	4,640,000	79	0.86	3,200	48.4	42.4	6.8

TABLE 3.—*Study of Blood Picture (Case 3)—Continued*

Date	Red Cells	Hemoglobin, per Cent (Sahli)	Color Index	White Cells	Polymorphonuclears, per Cent	Lymphocytes, per Cent	Monocytes, per Cent
10/13/32	4,310,000	71	0.82	3,000	65.6	32.0	2.2
10/19/32	4,500,000	70	0.78	2,600	64.0	28.0	7.6
10/25/32	4,410,000	62	0.70	4,000	64.0	30.4	4.0
11/ 2/32	4,410,000	70	0.79	5,800	63.2	31.2	4.0
11/16/32	4,510,000	74	0.81	2,600	51.2	36.8	10.4
11/30/32	4,410,000	73	0.83	5,400	61.0	31.0	5.0
12/29/32	4,620,000	69	0.75	5,200	56.0	33.2	8.8
3/29/33	4,630,000	74	0.80	3,800	74.8	20.8	3.6
4/12/33	4,310,000	65	0.75	4,200	53.6	40.4	4.8
4/26/33	4,350,000	61	0.70	5,600	66.4	26.4	5.6
5/10/33	4,160,000	67	0.82	4,300	62.8	30.4	5.6
5/24/33	3,950,000	71	0.91	4,100	57.6	35.2	4.8
6/15/33	4,450,000	73	0.82	5,000	60.8	33.6	3.2
6/16/33	4,290,000	76	0.90	4,450	72.8	22.4	4.0
7/13/33	4,840,000	80	0.83	2,600	60.8	33.6	4.8
8/10/33	4,370,000	73	0.83	3,600	64.0	31.2	3.2
9/ 7/33	4,130,000	76	0.93	5,000	60.0	33.2	6.0

The tuberculin reaction, repeated several times, was negative. The basal metabolic rate was +16.4, +20.8, +9.6 and +16.4 on four different trials. All other examinations gave negative results.

Under tuberculin therapy the lesions disappeared, but in February, 1932, scaly, flat, lupus erythematosus-like lesions occurred on the cheek. These responded to therapy with gold sodium thiosulphate.

The study of the blood picture was carried out for sixteen months. Analysis of the study shows red blood cells, hemoglobin and color index within normal limits. The leukocytes remained fairly high at first. Later they had a tendency to come down to lower normal levels.

The differential count during the period of leukocytosis showed an increase principally in the lymphocytes and the polymorphonuclear neutrophils; when the blood count reached normal the polymorphonuclears decreased to slightly below normal, while the other leukocytes remained virtually normal. This is a blood picture which also is not unusual in tuberculosis.

CASE 3.—*Tuberculosis of the Hypoderm, Wende.*—Mrs. C. C., an American housewife, 26 years old, was first examined on Dec. 10, 1930, on account of a disseminated eruption involving the face, neck, arms and legs of five years' duration. The eruption was composed of deep-seated nodules of various sizes, which varied in color from bluish to beefy-red. There was no tendency to ulceration; the healed lesions showed a depressed, pliable scar formation.

Evidences from histologic examination and animal inoculation proved this to be a case of tuberculosis of the hypoderm.

The study of the blood picture was carried out for thirty-three months. In this patient, too, the red blood cells, hemoglobin (although somewhat low) and color index remained at normal levels. The white blood cell count, however, showed a marked decrease, at times reaching as low as 1,200.

The differential count showed that the reduction occurred in all the leukocytes, but especially in the lymphocytes, with sufficient dipping of the curve to show a tendency to meet the monocytes.

CASE 4.—*Lupus Pernio (?) Sarcoid (?).*—Mrs. T. B. H., an American housewife, 53 years old, was first examined on July 16, 1931, on account of two per-

sistent, infiltrated lesions on her cheeks, of two years' duration. The lesions were of a dusky reddish hue and deeply infiltrated; they were covered with telangiectasias and showed a slight scaling. As the patient did not permit the taking of a section for biopsy, a positive diagnosis could not be made. Under treatment with tuberculin the lesions disappeared in about ten months.

The study of the blood was carried on for fourteen months.

Analysis of all these blood pictures indicates systemic disturbances, the simile of which may be found in patients suffering from systemic tuberculosis, for under various conditions generalized tuberculosis will

Fig. 5 (case 4).—Sarcoid of Boeck? Lupus pernio?

cause both leukocytosis, the type of blood picture seen in the patients with sarcoid, and leukopenia, the type shown by the other patients suffering from tuberculosis of the hypoderm.

This variance of blood picture in systemic tuberculosis depends on the type, species and number of tubercle bacilli, on the capability of the host to cope with the infective agent from the standpoint of immunity or on the lack of it and on the age of the process, and it is not unlikely that it also depends on climatologic conditions.

A study of the leukocytes in tuberculosis showed that these cells are an index of the activity of the pathologic process in the lesions. In active tuberculosis it is the rule to find leukocytosis, with an actual

increase in the polymorphonuclears and monocytes and an actual decrease in lymphocytes. Cunningham and Sabin [6] pointed out this relation between the lymphocytes and monocytes.

Medlar and Kastlin,[7] as a result of experimental work on tuberculous lesions by Medlar,[8] believed that the neutrophilic polymorphonuclear response in the blood in this disease gives additional information on the

TABLE 4.—*Study of Blood Picture (Case 4)*

Date	Red Cells	Hemoglobin, per Cent (Sahli)	Color Index	White Cells	Polymorphonuclears, per Cent	Lymphocytes, per Cent	Monocytes, per Cent
7/16/31	4,240,000	71	0.86	3,600	57.0	39.0	4.0
7/23/31	4,350,000	69	0.80	3,800	60.5	31.5	4.0
7/30/31	4,380,000	73	0.84	2,000	71.0	20.0	8.5
8/ 6/31	4,320,000	71	0.82	2,600	67.0	26.0	6.0
8/13/31	4,070,000	71	0.87	3,600	52.6	43.3	2.6
8/20/31	4,110,000	61	0.74	2,400	48.0	44.0	6.0
8/27/31	4,000,000	59	0.73	2,400	44.0	52.0	3.0
9/ 3/31	3,830,000	61	0.80	2,800	52.6	42.0	3.3
9/10/31	3,670,000	53	0.72	3,800	61.0	32.5	3.5
9/24/31	4,480,000	69	0.77	3,200	51.0	37.0	9.0
10/ 1/31	4,110,000	67	0.82	4,600	62.0	28.0	7.0
10/15/31	4,230,000	66	0.78	3,000	57.0	38.0	3.0
10/22/31	4,150,000	68	0.83	6,400	70.5	21.5	5.5
11/ 4/31	4,120,000	71	0.86	5,400	61.3	33.3	3.3
11/11/31	4,080,000	71	0.87	4,000	60.6	35.3	2.6
11/18/31	4,120,000	61	0.74	1,600	59.3	29.7	7.8
11/25/31	4,230,000	60	0.71	1,400	47.3	47.2	4.4
12/16/31	3,310,000	52	0.79	3,800	56.0	35.3	7.3
12/30/31	3,470,000	57	0.85	3,400	57.5	32.0	7.0
1/20/32	4,230,000	65	0.77	2,800	61.0	31.0	6.5
2/10/32	4,400,000	64	0.73	2,000	51.2	38.4	9.2
2/24/32	3,820,000	61	0.80	3,600	54.8	34.8	8.8
3/ 9/32	3,880,000	65	0.83	3,000	56.8	30.8	8.4
3/23/32	3,930,000	65	0.83	4,400	51.6	36.8	8.0
4/ 6/32	3,950,000	60	0.76	3,200	52.2	36.6	6.2
4/20/32	4,310,000	64	0.74	3,400	53.6	38.4	4.8
5/ 4/32	4,320,000	62	0.72	5,400	54.4	37.6	4.8
5/25/32	3,890,000	60	0.78	2,200	63.0	29.2	4.2
6/15/32	4,340,000	68	0.79	3,000	53.6	38.4	4.8
6/29/32	4,220,000	72	0.85	5,200	57.2	39.2	1.6
7/ 6/32	4,120,000	62	0.75	2,800	62.0	34.8	1.6
7/13/32	4,450,000	64	0.73	5,200	62.8	32.0	3.2
7/27/32	4,370,000	68	0.78	4,000	74.8	20.4	4.4
8/17/32	4,410,000	67	0.76	4,600	63.6	28.4	3.2
9/ 7/32	3,770,000	62	0.84	4,600	52.8	36.0	8.8
9/21/32	4,420,000	73	0.83	5,200	61.6	30.2	7.4
10/ 5/32	4,250,000	71	0.85	4,000	55.2	36.0	6.4
10/19/32	4,170,000	62	0.75	2,600	61.3	28.0	6.0
11/ 2/32	4,280,000	73	0.86	5,000	61.4	30.4	6.0

activity of the lesion. In healing tuberculosis, there is a decrease of the polymorphonuclears with an increase in lymphocytes, the monocytes remaining elevated. As healing progresses, the total number of leukocytes returns to normal or drops below normal. Generally speaking, it is believed that an increase in the monocytes and polymorphonuclears, with a decrease of lymphocytes, indicates extension and activity in

6. Cunningham, R. S.; Sabin, F. R.; Sugiyama, S., and Kindwall, J. A.: Bull. Johns Hopkins Hosp. **37**:231, 1925.

7. Medlar, E. M., and Kastlin, G. J.: Am. Rev. Tuberc. **16**:706, 1927.

8. Medlar, E. M.: Am. J. Path. **2**:275, 1926.

systemic tuberculosis. A decrease of polymorphonuclears and an increase of lymphocytes, usually with an increase of monocytes, denote a healing process. In low grade, inactive lesions, a persistent leukopenia with a tendency to an increase in lymphocytes is a common response of the blood.

This question of blood picture is another example of the protean nature of tuberculosis of which dermatologists are so well aware but which is not given sufficient emphasis, especially when it is contrasted with syphilis.

This observation seems to indicate that in the study of the blood picture there is another clinical manifestation of sarcoid which relates it to tuberculosis. One should include sarcoid under the heading of tuberculosis, recognizing it, however, as a distinct variety, maybe the product of a special or an attenuated strain of the bacillus, or occurring in persons whose reactions differ from the average, or both.

SUMMARY

1. Studies of the blood picture of four patients are recorded.

2. High basal metabolic rates are recorded in two cases of sarcoid of Boeck.

3. Further arguments are raised for the classification of sarcoid under tuberculosis.

631 Jenkins Building.

TUBERCULOSIS OF THE SKIN

A CLINICAL REPORT

JOHN E. RAUSCHKOLB, M.D.
CLEVELAND

During the decade 1922 to 1932, there were 115,649 patients admitted to Cleveland City Hospital. There were 6,399 diagnoses of tuberculosis of various types made within this period. Ordinarily the dermatologic service is requested to examine any of these patients with unusual lesions of the skin. If they are extensive, it is possible that the patient is admitted to the dermatologic service. Otherwise it is certain that sometimes in the other services cutaneous manifestations of tuberculous origin have not been especially noted, and that at times their true character has not been elucidated. That, at least, is an explanation for the small number of cases discussed in this report. Among 6,399 patients with tuberculosis, 68 were recognized as having tuberculous manifestations of the skin or mucous membrane or of both.

CLASSIFICATION OF CASES

To facilitate the study and correlation of findings, it seemed desirable to group the various types of cutaneous tuberculosis according to the classification of Lewandowsky. The series of 68 cases was divided into two groups, one manifesting itself in localized lesions, the etiology of which was either primary contact or secondary infection from a focus in the body, and the other revealing itself as a more or less generalized process of hematogenous origin.

In the group of so-called localized lesions there were 34 cases: 1 case of verruca necrogenica in a physician following a cut on the finger while doing an autopsy on a tuberculous subject, 6 cases of lupus vulgaris, 5 cases of tuberculosis verrucosa cutis and 5 cases of tuberculosis colliquativa. There were 589 cases diagnosed as glandular tuberculosis among the group of 6,399 patients exhibiting tuberculosis in one form or another. It has certainly seemed noteworthy that only 4 authentic cases of tuberculosis colliquativa were recorded in this group of tuberculous glandular involvement.

Read at the Fifty-Sixth Annual Meeting of the American Dermatological Association, Inc., Chicago, June 9, 1933.

From the Dermatological Department of Cleveland City Hospital and from the School of Medicine of Western Reserve University, service of Dr. Cole and Dr. Driver.

There were 17 cases of ulcerative tuberculosis of the skin and mucous membranes. In 11 the tongue was involved: in 4 on the anterior part, in 4 at the base, and in 3 the location was not noted. In 4 of these cases the tongue alone was involved, while in 7 the adjacent mucous membrane was also affected. In 1 of these the upper lip likewise showed ulceration. In 2 cases the tonsils and adjacent structures were involved. There was 1 case of tuberculosis of the lower lip and buccal mucosa and 1 of tuberculosis of the hard and soft palates. In 1 instance there was an ulceration at the angle of the mouth extending out onto the skin. In the final case in this group there was an extensive ulceration of the rectum extending forward into the tissues of the left buttock. All the cases of involvement of the mucous membrane were secondary to tuberculosis of the lungs, and in 13 of them tubercle bacilli were found in the sputum. It is possible that with long enough observation the sputum in all 17 cases would have been positive for tubercle bacilli. With the exception of 2 cases of tuberculosis colliquativa in which there were lesions below the waist—1 on the knee from periostitis and 1 in the inguinal region from involvement of the inguinal nodes—and a case of ulcerative tuberculosis of the mucous membrane that involved the rectum and perianal tissues, all the cases grouped in the first primary subdivision of localized lesions involved the face, neck, head or upper extremities.

In the group of lesions of hematogenous origin there were likewise 34 cases: lichen scrofulosorum, 11 cases; papulonecrotic tuberculid, 17 cases; erythema induratum, 2 cases; sarcoid of the Darier-Roussy type, 1 case; the so-called multiple sarcoid-like granuloma of the skin, described by Klauder and Weidman,[1] 2 cases, and tuberculosis of the hypoderm, described by Wende,[2] 1 case.

In this second group, the great majority of the patients exhibited generalized lesions. This was not true of the 2 patients with erythema induratum with lesions on the lower extremities. One of these also displayed a tuberculous dactylitis.

It is remarkable from an ophthalmologic standpoint that more than 50 per cent of the patients with lichen scrofulosorum also demonstrated phlyctenular conjunctivitis. Twenty-five per cent of the patients with papulonecrotic tuberculid likewise showed this syndrome.

---

1. Klauder, J. V.: Multiple Sarcoid-Like Granulomas of the Skin of Undetermined Nature, Arch. Dermat. & Syph. **12**:171 (Aug.) 1925. Klauder, J. V., and Weidman, F. D.: Multiple Sarcoid-Like Granulomas of the Skin of Undetermined Nature: Supplementary Note, Arch. Dermat. & Syph. **13**:675 (May) 1926.

2. Wende, G. E.: Nodular Tuberculosis of the Hypoderm, J. Cutan. Dis. **29**:1, 1911.

It is not possible to explain the remarkably small number of cases diagnosed as erythema induratum. The 2 cases in the series were the only ones in the dermatologic service.

All dermatologic patients suspected of having a tuberculous etiology are studied by means of tuberculin tests. The practice in the service is to start the intradermal injections with a dilution of 1 : 1,000,000, continuing gradually and with great caution down to a dilution of 1 :100, if necessary, before recording a negative result. Earlier initial injections of 1 :1,000 strength in 2 cases of papulonecrotic tuberculid in children were attended by marked febrile reactions, ulcerations at the site of injection and finally a generalized exfoliating dermatitis. The intradermal tuberculin reactions and accessory laboratory data were recorded in 44 cases. The largest single group of patients exempted from this test was the 17 with ulcerative tuberculosis of the skin and mucous membranes on whom it was entirely omitted. This was intentional as all the patients were adults in the advanced stages of the disease. The reaction was positive in 31 cases and negative in 13. The groups of patients with lichen scrofulosorum, lupus vulgaris and erythema induratum contributed 100 per cent positive reactions. The group with papulonecrotic tuberculids exhibited 96 per cent positive reactions. In some instances the dilutions were low, but as a rule in these cases and in lichen scrofulosorum the reactions were positive in high dilutions. Sixty per cent of the patients with tuberculosis verrucosa cutis had positive reactions. An anergy was noted in the one case of multiple sarcoid-like lesions and a positive reaction in the other in a dilution of 1 : 1,000, but in the case of tuberculosis of the hypoderm there was a frankly positive reaction.

Biopsies were done in 37 instances. In every instance routine examination of the tissue was made for acid-fast organisms. Naturally, in a busy city hospital with lack of help, it is not possible to spend a long time in searching sections for such organisms. Tubercle bacilli were found in 4 cases: 1 case of verruca necrogenica, 1 of lupus vulgaris, 1 of tuberculosis colliquativa and 1 of tuberculosis of the hypoderm, as described by Wende. The histopathology was considered definitely diagnostic of tuberculosis of the skin in 28 cases and suspiciously diagnostic in 3 cases. In 11 cases no diagnosis of tuberculosis could be made, and the report of nonspecific granuloma was returned. Inoculation into guinea-pigs was performed in 6 cases and inoculation into chickens in 2. Both inoculations were done in the 2 so-called cases of multiple sarcoid-like granuloma of the skin described by Klauder and Weidman. The inoculations into the chickens were done in view of the possible participation of avian tubercle bacilli in the etiology of the disease. Inoculations into both guinea-pigs and fowls were negative. Two other inoculations into guinea-pigs, performed in a case of ery-

thema induratum and a case of tuberculosis colliquativa, were negative. Two positive inoculations into guinea-pigs were reported, one in a case of tuberculosis verrucosa cutis and one in the case of tuberculosis of the hypoderm.

Wassermann reactions were recorded in 60 of the 68 cases, of which 58 were negative and 5 were positive. One of the positive reactions was obtained in a case diagnosed as ulcerative tuberculosis of the tongue and buccal mucosa. This patient died four days after admission, and autopsy was performed. No evidence of syphilis appeared on pathologic examination. The other four positive reactions occurred in the papulonecrotic and lichen scrofulosorum groups. The positive Wassermann reactions among the patients with lichen scrofulosorum occurred in 2 Negro girls under 3 years of age. The only objective symptoms suggestive of syphilis were the positive Wassermann reactions. In the 2 cases of papulonecrotic tuberculid with positive reactions, the patients were Negroes, aged 36 and 40 years, respectively. In both the diagnosis of latent syphilis was also made. One patient received eight injections of a soluble bismuth preparation with no improvement of the cutaneous process. The other patient received sixteen injections of a soluble bismuth preparation and two injections of arsphenamine with similar failure to improve the papulonecrotic eruption.

OTHER ETIOLOGIC FACTORS

Roentgen examination in 66 of the cases showed definite pulmonary tuberculosis in 45, doubtful involvement in 1 and negative findings in 20. Tubercle bacilli were found in 19 of the 40 cases in which examinations of the sputum were recorded. Eighty-one per cent of the patients in the group with localized lesion showed pulmonary tuberculosis. The patients in the group with the ulcerative type of tuberculosis of the mucous membrane augment this figure definitely, since 100 per cent exhibited active tuberculous infection of the lung. In other words, the cases of tuberculosis of the mucous membrane were all secondary. Fifty-four per cent of the patients with lesions of hematogenous origin showed the same pathologic process. The group of patients with papulonecrotic tuberculid were the heaviest contributors in this division, 60 per cent showing roentgenographic evidence of pulmonary tuberculosis.

In this series of 68 cases there were 45 males and 23 females. There were few conspicuous findings as to preference of any type of the disease for one sex or the other with the notable exception of the group of ulcerative forms of tuberculosis of the skin and mucous membranes. Here there was a definite and heavy preponderance of males, the proportion being 7.5 : 1. Ten of the eleven cases in which the tongue was involved occurred in males. This confirms the observation made by

Morrow and Miller.[3] A definite preference for the male sex seemed likewise apparent in the group having papulonecrotic tuberculid.

As to race, there were 30 white and 38 Negro patients. This is a relatively high proportion of Negroes, since the proportion of white to black persons in Cleveland is approximately 14 : 1. This finding was of no unusual interest, though, in the face of an acknowledged susceptibility of the Negro race to tuberculous infection. There was, however, a significant and consistent preference of the white race for those forms of cutaneous tuberculosis manifesting themselves in more or less localized lesions. The ratio of white patients to black patients in this general group was 3 : 1. Conversely, the Negro race exhibited an even greater predilection for those types of tuberculosis of the skin considered as of hematogenous origin. The proportion in this instance was 7.5 Negro patients to 1 white patient.

The modal age of the total series was computed to lie between the second and third decades. This, however, was seen to be of little more than statistical value. Twenty-five of the 68 cases occurred in the first decade of life, and two thirds of these were in children under 5 years of age. All the cases of lichen scrofulosorum occurred in the first decade. It is important to note that 22 of the 25 cases occurring in early childhood belonged to types considered of hematogenous origin. Fifty-four per cent of the cases of the papulonecrotic type occurred within the first ten years of life. Another 25 per cent of this group occurred in the third decade.

Sixteen of the total 68 cases were found to occur between the third and fourth decades. Here the ulcerative form of tuberculosis involving the mucous membrane was the heaviest contributing factor. Forty-three per cent of the cases in this age group were of this form. There were 2 cases in the fifth decade.

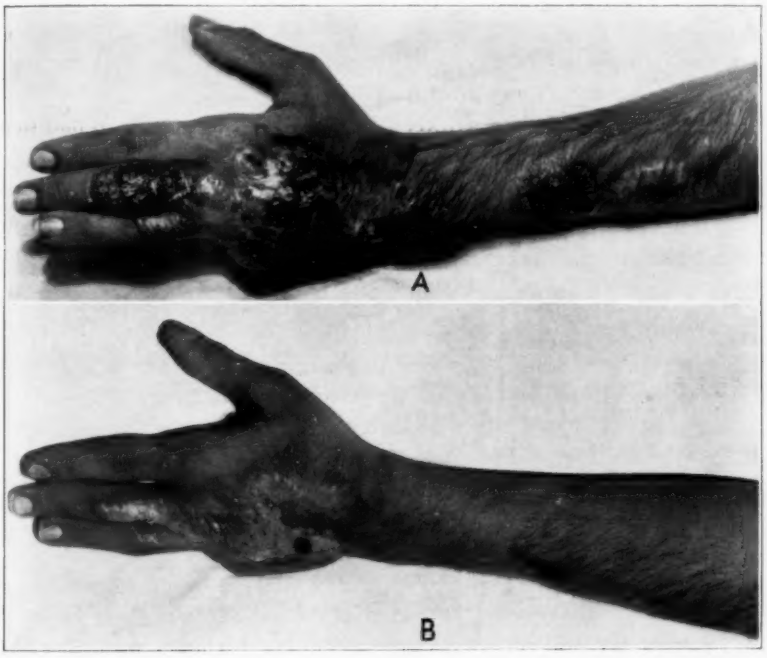
END-RESULTS AND TREATMENT

Twenty-five per cent of the total series of patients died. In each instance death was due to pulmonary tuberculosis. The heaviest mortality rate was found in the group with ulcerative tuberculosis of the mucous membrane, in which 66 per cent died. Many of these patients with advanced pulmonary tuberculosis were seen in consultation while being confined to the hospital sanatorium. Twenty-five per cent of the series of patients were discharged unimproved.

Fifty per cent of the group were discharged as improved or healed. The various therapeutic measures generally advocated, x-rays, radium,

3. Morrow, H., and Miller, H. E.: Tuberculosis of the Tongue, J. A. M. A. **83**:1483 (Nov. 8) 1924.

excision, injections of gold and bismuth preparations and of arsphenamine and general hygienic and supportive measures, were used as seemed most appropriate. No particular form of therapy was felt to be of unusual or specific value outside of the procedure described as curettage and impregnation with powdered potassium permanganate. This was suggested in 1926 by Auregan,[4] though Darier, in discussing Auregan's paper, said that it had been described at an earlier date. Four patients with lupus vulgaris and 4 with tuberculosis verrucosa cutis were treated



A, case of tuberculosis verrucosa cutis before therapy; *B*, final results following curettage and impregnation with powdered potassium permanganate.

according to this technic. Five of these 8 patients were discharged as improved and 3 as healed. The procedure required the use of general anesthesia. The lesions healed slowly and with some pain. There were no toxic symptoms from the potassium permanganate. The final result from the cosmetic standpoint was excellent. With these exceptions, the patient with verruca necrogenica treated by excision and x-rays was the only other one in the series of 68 patients discharged as healed.

4. Auregan, M.: Traitement du lupus par curéttage et imprégnation au permanganate de potasse finement pulvérisé. Résultats de cette méthode appliquée depuis vingt ans, Bull. Soc. franç. de dermat. et syph. **33**:44, 1926.

CONCLUSION AND SUMMARY

1. A statistical report is presented on a series of 68 cases of tuberculosis of the skin and mucous membranes seen in a large city hospital from 1922 to 1932.

2. The cases are divided into two groups, those manifesting themselves by localized lesions and those of hematogenous origin.

3. The white race was the heavier participant in the group with localized lesions whereas the black race was even more preponderantly represented in the types of hematogenous origin.

4. Thirty-seven per cent of the cases occurred in the first decade of life, more than 90 per cent of this number belonging to the group considered as of hematogenous origin.

5. Sixty-one per cent of the total group had demonstrable pulmonary tuberculosis. Included here are 100 per cent of the cases of ulcerative tuberculosis of the skin and mucous membranes.

6. More than 50 per cent of the patients with lichen scrofulosorum exhibited phlyctenular conjunctivitis. Twenty-five per cent with papulonecrotic tuberculids also showed this syndrome.

7. Twenty-five per cent of the entire series died, in each instance of pulmonary tuberculosis; 25 per cent were discharged unimproved, and 50 per cent were discharged as improved or healed.

8. In a group of patients with lupus vulgaris and tuberculosis verrucosa cutis, curettage of the lesions followed by impregnation of powdered potassium permanganate yielded favorable results.

ABSTRACT OF DISCUSSION

ON PAPERS OF DR. MICHAEL AND DR. RAUSCHKOLB [5]

DR. HENRY E. MICHELSON, Minneapolis: This subject is so extensive and I have so many thoughts on it that I am sure I shall be able to touch on only a few of them. From the study of our own cases of granuloma annulare, I do not feel like grouping them with tuberculosis at the present time. I well realize that so great an authority as Professor Jadassohn has included this condition in his classification of the tuberculodermas.

I feel that the entire subject of tuberculin tests as done by dermatologists needs an airing. Dr. Sweitzer and I have been attendants at a large county tuberculosis sanatorium for a good many years, and we have watched the work with tuberculin and feel that conclusions can be drawn only when the tester is entirely familiar with his product, dilutions, time of reaction and, above all else, a technic that is carried out with meticulous care.

One must not speak of tuberculous histology, for we all know that there is no histology that is pathognomonic for tuberculosis. As has been so fully pointed out, tuberculoid structure can be caused by many different conditions. If one makes sections from a known case of tuberculosis of the skin over a period of months, one will be greatly surprised to find that the picture varies rapidly and

5. Michael, J. C.: Etiology of Granuloma Annulare, with Special Reference to the Tuberculous Therapy, Arch. Dermat. & Syph. **29**:189 (Feb.) 1934.

that lesions which are similar clinically in the same person may be entirely different microscopically. Therefore, a decision can be arrived at only from a sum total of the knowledge gained from these examinations. I believe that it is a mistake to consider granuloma annulare as a condition which has a fixed pathology, for the central necrosis is not always present, and the early changes are quite unspecific. Results of tuberculin therapy do not impress me much with regard to etiology, for I look on this form of treatment as a form of foreign protein therapy.

Steiner, of Professor Kren's clinic, views granuloma annulare as a disease of multiple origin.

The simultaneous appearance of various types of tuberculous lesions in the same person always is extremely interesting, and in the case mentioned by Dr. Michael one must not forget the possibility of a tuberculide en plaque such as that described by Dr. Sweitzer. In his case the lesions looked surprisingly like granuloma annulare. For my own part I think that the etiology of granuloma annulare must still be looked on as unknown.

The paper of Dr. Rauschkolb is exceedingly good, and Dr. Cole, I am sure, must be much gratified to have such a good summary of the cases of tuberculosis in his service. The gathering of statistics on tuberculosis of the skin is important and is much more difficult in this country than in Europe because there are so few cases. Roughly speaking, in the same length of time in the Jadassohn Clinic there would have been about 2,000 cases of tuberculosis of the skin and in the large Vienna clinic about 600 cases, so one must turn to the Continent for opinions on this disease.

I think one should be careful about the use of terms, for example, inoculation tuberculosis of the skin or hemotogenous tuberculosis of the skin. All tuberculosis is inoculation tuberculosis no matter how the inoculation is made. It is possible to discuss how a germ arrives at a particular site, but there is no definite way of concluding just where it came from. It is always so important to make certain whether or not a focus of tuberculosis exists in other parts and this, of course, is most difficult to do. One knows that bacillemia is possible and that a patient may have tubercle bacilli circulating in his blood and still be clinically well. Therefore hematogenous dissemination is not the reason why a certain type of tuberculosis develops. Another question that is hard to answer is whether the infection is from without or from the patient's germs. One must think of external and not exogenous infection, just as one speaks of internal and not endogenous inoculation. Another important point is the fact that nutrition in a large way must play an important part. Even if the salt-free diet becomes discredited, there is enough proof at hand to show that what a patient eats and how he lives must make a tremendous difference in his susceptibility to tuberculosis.

Dr. Fred D. Weidman, Philadelphia: Dr. Michael and Dr. Michelson have given a perspective of the theories as to what granuloma annulare may be due to. The point that I want to discuss is that if the condition is not always tuberculosis but may be something else, what may that "something else" be? Perhaps I may be of service to dermatologists if I cite the reaction of a general pathologist at his entrance into dermatology. When I first became associated with Dr. Milton B. Hartzell's clinic, he turned over to me a goodly portion of his histologic sections, among them one of granuloma annulare. At that time I had never seen a case of granuloma annulare clinically. I had had ten or twelve years' experience as a full time worker in general pathology at the University of Pennsylvania. When I first saw his sections of granuloma annulare, tuberculosis did not occur to me as the diagnosis; incidentally, the section I studied is reproduced in Hartzell's textbook. There was a large focus of central necrosis with just a scattering of spindle cells peripherally. In short, my first impression was that granuloma annulare was simply a large-sized focal necrosis. Since then I

have seen cases of erythema elevatum diutinum and other diseases, for example, rheumatism of the aorta, in which focal necrosis is also produced and in which spindle cells are found and even some Aschoff-like cells, which are so well known in rheumatism and involve the streptococcus. After additional similar experiences with sections of granuloma annulare, I have been a strong adherent of the theory of the nontuberculous causation of at least some cases of granuloma annulare. The point is, that just as there is no fixed histology for tuberculosis (as Dr. Michelson said), there is none for streptococcus infections. They vary widely and give differing reactions.

The question remains as to how the streptococcus may be productive of this type of lesion. Recalling the histology of the rheumatic dermatoses in general, one can readily understand how granuloma annulare may fundamentally be but local multiple infarcts in the skin. Imagine a mural thrombosis of one of the cutaneous arterioles, succeeded by repeatedly developed thromboses in its peripheral twigs as the result of streptococcic emboli. These are blocked off, and little areas of necrosis (infarcts) result.

This could account for the histopathology, but another question remains, namely, Why should they have an annular configuration? By way of comparison, one may recall the effect given by infarcts of the spleen and kidney as viewed on the capsular surface, i. e., central, more or less depressed areas with a surrounding zone of collateral hyperemia. Here the central area of coagulation necrosis would compare with the central depressed area (really focus), and the reactive zone of collateral hyperemia would compare with the raised border of active tissue reaction in granuloma annulare. Similar thoughts were expressed by Professor Jadassohn when delivering his address on the hematogenous dermatoses at the Del Monte meeting of this association.

In short, I can understand how embolism or thrombosis can affect the smaller arterial twigs in a ringlike manner as they approach the surface and induce multiple microscopic infarctions. I should not contend that it is the streptococcus alone that can produce this effect. In erythema nodosum the tubercle bacillus can produce effects clinically similar to those of rheumatic agents; when these organisms are considered as they elicit such different kinds of tissue response, I think that something else than tuberculosis enters into the formation of the lesions of granuloma annulare, and that one of the factors to be admitted is streptococcic (and perhaps even sterile) infarction.

Dr. Robert C. Jamieson, Detroit: I was particularly interested in Dr. Michael's discussion of granuloma annulare on account of a patient recently seen, whose case may perhaps clarify the complicated situation. This patient has been treated for a number of years for erythematous lupus. Her lungs were normal, and she had probably had tuberculin tests before I saw her, as she is the sister of a physician. She had a sinus infection which cleared up several times following treatment with a gold compound. She returned with a lesion of granuloma annulare on the site of one of the former lesions of lupus erythematosus. A gold preparation did not affect this. The condition cleared up under roentgenotherapy, and she thinks she cleared it up with yeast.

In this case I would be inclined etiologically to diagnose the lesion as toxic rather than tuberculous.

Dr. William H. Guy, Pittsburgh: Dr. Pollitzer asks me to refer to 2 cases of granuloma papulonecroticum of more or less generalized type in which tests for tuberculosis gave negative results and in which we recovered the colon bacillus from lesions. Both patients suffered from marked visceroptosis and obstipation.

In a period of remission of lesions, small doses of colon bacilli were injected intracutaneously and subcutaneously. Through an error we gave too large a dose and precipitated an attack of granuloma papulonecroticum; the patient was quite ill for some time. Treatment was directed toward the intestinal tract with a diet rich in roughage, support of the abdomen and corrective exercises. The condition cleared up entirely in 1 case and there has been no recurrence to date. One patient improved somewhat, but has had recurrences from time to time.

This is only suggestive evidence that granuloma papulonecroticum may be due to a variety of organisms of feebly pathogenic powers disseminated from a focus of infection, as in these cases from the intestinal tract, localization being determined to some extent by a weak peripheral circulation. I may say that I have not been able to duplicate these findings in other cases of granuloma papulonecroticum.

Dr. Harold N. Cole, Cleveland: I am glad to hear Dr. Michelson's comments on the tuberculin test. I think that as it is often carried out it has little value. However, when employed with scrupulous cleanliness and when constantly checked, it is of great value. In our department we check constantly with the department for tuberculous patients. The test is begun with 1: 1,000,000. One can get a good idea of the patient's allergy, and it is of great value in controlling the patient's course. Moreover, we have found that in papulonecrotic tuberculid if one starts in with doses of 1: 1,000 there may be a disastrous result. We have had one or two such occurrences. It is very necessary to start with a weak dilution in patients with high allergy or one may get into difficulty.

Dr. Jeffrey C. Michael, Houston, Texas: The discussion has been illuminating and has stressed points that puzzle me considerably.

Dr. Michelson mentioned the point that thorough examination for systemic tuberculosis should rule out that disease. I do not agree with that, and I have recently heard Dr. Allen Krause remark that discovery of tuberculous infection may escape the most painstaking examination.

So far as the relationship between tuberculosis and granuloma annulare is concerned, I have been more impressed with clinical than with laboratory evidence. The latter probably speaks against the tuberculous etiology of granuloma annulare, but the clinical association of active tuberculosis and granuloma annulare is striking. I cannot criticize the diagnosis of men like Carol and Mendes da Costa.

The conclusions I came to were not satisfactory, but I believe they are logical deductions from present-day evidence. I am inclined to regard granuloma annulare as due to tuberculosis more often than to any other cause. Dr. Weidman's suggestion that streptococci or other bacteria may be responsible for some cases is in line with my conclusions.

MULTIPLE EPITHELIOMAS AND PIGMENTARY DERMATOSIS IN A NEGRO BOY

RALPH HOPKINS, M.D.
AND
M. T. VAN STUDDIFORD, M.D.
NEW ORLEANS

The case reported in this paper is the first case of epithelioma seen in a large and long-established clinic for Negroes at Charity Hospital in New Orleans. Conversations with dermatologists who have clinics attended by Negroes in other cities have confirmed our belief that cancers of the skin rarely if ever occur in Negroes. The interest of the case lies, it is thought, not only in the fact that epitheliomas with very destructive tendencies occurred in a child of a race naturally immune to cutaneous cancers, but also in the character of the dermatosis to which the epitheliomas apparently were a sequence.

REPORT OF A CASE

Race.—By the word Negro it is meant that the patient had all the Negro characteristics. His skin was black and his hair "kinky," and his general appearance was such that he created the impression of being a full-blooded Negro. He was, however, not entirely of African descent.

All of his ancestors on the paternal side were, as far as his genealogy could be traced, full-blooded Negroes and Negresses. His maternal grandmother also was a full-blooded Negress, but his maternal grandfather was a mulatto whose mother was a full-blooded Negress, but whose father was a white man. Of the patient's eight great-grandparents, therefore, one was white and the remaining seven were full-blooded Negroes or Negresses. In conformity with the racial history of the child's parentage, the mother's skin was notably lighter than that of the child. It was stated that on the mother's side of the family there had been some relatives with a trace of dusky red hair. Examination of the mother's skin disclosed some pigmented moles, but no freckles.

History.—A Negro boy was 5 years old at the time of his admission to Charity Hospital in July, 1932. The history given by the boy's mother was that at birth he was a normal baby, and that he had a normal physical development for the first few months of life, during which time his skin was unblemished.

When the child was 6 months of age, his mother took him out in the fields with her while she picked cotton. He was exposed to the sun all during the day, and that night high fever and convulsions developed. A physician was called; he told the mother that her baby had "anemia of the stomach" and gave treatment, with no results. The child was sick for several months, and three or four times during this period he passed bright red blood in his stools.

Read at the Fifty-Sixth Annual Meeting of the American Dermatological Association, Inc., Chicago, June 8, 1933.

When he was about 1 year old, the mother noticed a pea-sized black spot on the child's nose which was followed by more spots until the entire face was "speckled." About this time a small tumor developed on the left lower eyelid, which the mother described as "warty-like" in character. Because of this growth, she felt that his eyes were weak and did not expose him to unnecessary sunlight. The physician applied a salve to this tumor, and it disappeared within a few weeks. Shortly after this, a dark brown wart developed on the nose which grew rapidly and projected about 1 cm. above the surface of the skin. The child was carried to a hospital, where the growth was removed. Following this, the mother noticed that black spots had appeared over the neck, arms, hands and legs. She tried to remove the spots with a salve obtained from a local drug store, but accomplished nothing beyond irritation of the skin.

At the age of 4, the patient had sores on the face, some of which healed, while others continued to appear. As all of these sores healed spontaneously after several months, and as the child had no more lesions of this character, it is more probable that they were due to impetigo than that they were a part of the history of the pigmentary dermatosis.

At the age of 4½ years, three or four tumors developed on the face, which projected from the surface of the skin and grew rapidly. Most of these tumors broke down and formed large ulcerated areas over the face, while those remaining continued to increase in size. The ulcers also had been steadily progressive.

The child had never complained of pain from the local condition, but had had frequent headaches for a week before his admission to the hospital.

The patient's mother stated that the child had never received any medication with arsenic. However, he had lived on a cotton farm on which an insecticide containing arsenic was used for destroying parasites, and some of this insecticide was kept in open cans in an outhouse to which the child had easy access and in which he often played. She also stated that the child often played in a field in which arsenic had previously been sprayed on the cotton bushes.

The mother stated that no members of her family had been subject to diseases of the skin of any kind.

The child was admitted to Charity Hospital in July, 1932, and notwithstanding treatment with radium, he grew progressively worse and died in November of the same year.

Description.—On admission the most conspicuous abnormalities of the skin were tumors and ulcers on the face. In addition to these lesions, which were present only on the face, there was a more generalized condition of hyperpigmentation and depigmentation associated with scales and atrophy. This dermatosis was symmetrical in distribution and occurred almost exclusively on the exposed surfaces.

The Epitheliomas: The largest of the tumors was on the forehead to the left of the median line and over the orbital region. This mass, in which there was no ulceration, was 3 or 4 cm. in diameter and was elevated about 1 cm. above the surrounding skin. There were smaller tumors varying in diameter and elevation and lesions resembling senile keratoses in varying degrees of development.

The ulcers on the face varied from 3 to 5 cm. in diameter. The largest ulcer occupied nearly all the central portion of the face, including the nose, which was almost entirely destroyed, and the cheeks in which destruction of tissues extended to a depth sufficient to expose the cavities of the antrums. The nasal passages were also exposed, and in the ulcerated area there remained irregular protruding

Fig. 1.—Arsenical pigmentation showing relative and absolute hyperkeratosis and spotted pigmentation of the cell layer. (Photomicrographs by courtesy of Dr. O. E. Denney.)

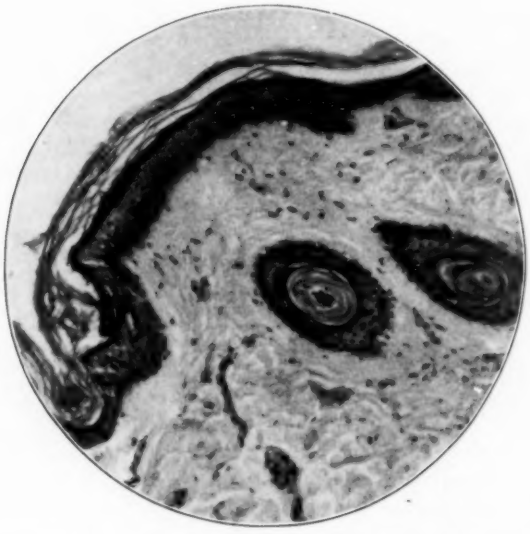


Fig. 2.—Arsenical pigmentation showing relative hyperkeratosis, spotted pigmentation, pyknosis and palisade arrangement of the basal cells; also atrophy of the prickle cell layer in certain areas.

masses of bone and cartilage. Two smaller ulcers were present on the upper right side of the face, one on the forehead near the outer part of the orbit, and the other near and anterior to the upper part of the ear. Both ulcers were comparatively shallow, not more than 0.25 cm. in depth. Their bases showed little evidence of sloughing tissue and were smooth. Parts of the borders of both ulcers had rolled edges. In none of the areas in which ulceration had occurred was there any evidence of healing, nor was there any scar tissue from previously healed lesions. All of the ulcers showed a marked tendency to bleed when being dressed. The eyeballs apparently were not involved in the malignant process, but the child showed evidences of a considerable degree of photophobia. There was no nystagmus.

The clinical appearance of the tumors and ulcers on the face was typical of epitheliomas in varying stages of advancement and ulceration. Some of the lesions were suggestive of the basal and some of the squamous cell type.

The Dermatosis: The generalized dermatosis showed a marked predilection for the exposed surfaces, and in each of these regions it occurred to the greatest extent on those parts of the region which were most exposed. The lesions were found in gradually diminishing numbers and degrees of severity between the parts subjected to the greatest and those subjected to the least exposure. There was no definite line of demarcation between the affected regions and the normal skin.

The dermatosis was more marked on the face than on other anatomic regions. On those parts of the face in which tumors and ulcers had not developed, there were scaly patches from 2 to 5 mm. in diameter, blue-black pigmented areas 4 or 5 mm. in diameter and smaller areas which were depigmented. No part of the skin of the face appeared normal; all of the unulcerated surface had an atrophic, rough, scaly or "speckled" appearance.

On the neck the dermatosis was similar to that on the face, but the lesions were less numerous and less highly developed, and normal skin could be detected between the abnormal patches.

The lesions on the shoulders and in the regions over the clavicles and upper part of the sternum were fewer and in a less high degree of development than those on the face and neck. The upper unexposed surfaces of the trunk presented few lesions, and the lower part was not involved to an appreciable extent.

On the arms, hyperpigmentation and depigmentation were the most conspicuous lesions. The freckled appearance was augmented by the depigmentation which occurred in spots of about the same size and in the same number as the freckles. Both types of lesions were small (2 or 3 mm. in diameter) and circular, but were so numerous on the more exposed parts of the arms that there remained comparatively little of the normally pigmented skin. The axillae and adjacent aspects of the arms were not involved, and the lesions were more prominent in the region of the deltoids and the extensor surfaces of the forearm, in which areas the epidermis was rough and scaly. Scattered more sparsely than the brown freckles over the arms were small (several millimeters in diameter) macules of a blue-black hue. The palmar surfaces, in contrast with the dorsal, did not appear atrophic, nor were they scaly and rough, but each presented a few light brown freckles.

On the upper part of the thighs the only lesions found were small and sparsely scattered white macules 1 or 2 mm. in diameter. From the lower part of the thighs downward to the knees, freckles and depigmented spots became gradually more numerous, and from the knees to the dorsal surface of the toes, the skin

Fig. 3.—Arsenical pigmentation. Note the hyperkeratosis, atrophy of the rest of the epidermis, pyknosis, vacuolation of the basal cells, spotted melanin pigmentation in the basal cells of the epidermis and many chromatophores in the upper cutis laden with pigment. Silver nitrate and hematoxylin stain.

Fig. 4.—Hemangioma and low grade squamous cell epithelioma with marked pearl formation. Hematoxylin and eosin stain.

had the "speckled," roughened, scaly and atrophic appearance seen on the arms. The soles were free from all lesions.

Laboratory Findings.—The blood chemistry was normal. The red blood cells were reduced to 3,800,000. The white blood cells totaled 9,300, with 4 per cent eosinophils. The hemoglobin was reduced to 60 per cent. Two Wassermann blood tests were negative, as was also one of the mother's blood.

The urine was normal except for occasional white blood cells. The renal function showed no impairment.

Roentgenograms showed normal pulmonary areas and no evidences of metastasis.

Biopsy (Dr. E. Von Haam and Dr. John H. Connell) showed squamous cell carcinomas.

Fig. 5.—Multiple squamous cell epitheliomas in a Negro boy.

The autopsy report of Dr. Von Haam and Dr. Connell recorded no metastasis to the lymph glands nor any significant pathologic changes in the internal organs except bronchopneumonia (probably due to aspiration) and severe colitis. Their report, in part, read: "The small intestine is free of pathologic changes. The mucous membrane of the large intestine shows extensive areas of necrosis and ulceration, covered with a fibrinous membrane. Almost the entire membrane is destroyed and only a few islands of intact mucosa remain. The changes are most marked in the descending colon." Dr. Von Haam and Dr. Connell were inclined to believe that the ulceration was more superficial than would be expected from the ingestion of arsenic. (The fact that there were no symptoms of intestinal derangement until several weeks before the child's death is confirmatory of the opinions of Dr. Von Haam and Dr. Connell.)

"Microscopic examination of sections through the colon shows extensive ulceration of the mucosal membrane. The ulcers are flat and do not extend far

into the sub-mucosal layer. The bottom of the ulcer is formed by leucocytes and lymphocytes."

Microscopic examination of sections through the skin of the face, made post mortem, confirmed the biopsy finding of squamous cell epithelioma. Dr. Von Haam and Dr. Connell found those sections in which malignant processes had not occurred in conformity with what might be expected in xeroderma pigmentosum.

Histopathologic Changes.—Dr. Hamilton Montgomery made and examined sections from different types of lesions taken for biopsies, and subsequently a section of skin removed post mortem.

His findings were summarized as follows:

"Biopsy Number 1: Sections from the leg do not show any definite evidence of xeroderma pigmentosum but are quite suggestive of arsenical pigmentation. In xeroderma pigmentosum the rete ridges are long and narrow and the epidermis between them is often atrophic. In only two areas in this section was there any attempt at proliferation of the rete ridges and even here the epidermal changes are more like those seen in arsenical pigmentation than in xeroderma pigmentosum. In this section there is a mild acanthosis which would be consistent with

Fig. 6.—Arsenical pigmentation of the palms.

the development of early arsenical keratoses. The slides show relative and absolute hyperkeratosis with atrophy of the prickle cell layer in some areas, hyperkeratotic plugging both in relation to and independent of hair follicles and sweat ducts, pyknosis and palisade-like arrangement of the basal cell layer in many areas, edema of the papillary bodies, some obliteration of the rete ridges, dense deposits of melanin pigment both in the epidermis and in the chromatophores in the cutis which is more marked than the normal amount seen in Negro skins, and, finally, a mild perivascular infiltrate in the upper cutis, composed chiefly of lymphocytes. The combination of these histologic findings strongly suggests an arsenical pigmentation.

"Biopsy Number 2 taken from the face shows the histologic picture of a squamous cell epithelioma, grade II, according to Broder's classification. In many places there was marked individual cell keratinization and in other areas the development of an epithelioma in situ presenting many dyskeratotic cells, clumping of cells, and giant epithelial cells simulating the picture of Bowen's disease. Epitheliomas resulting from the use of arsenic are usually squamous cell and are often quite malignant in character. The development of squamous cell epitheliomas in this patient could readily be explained on the basis of arsenic pigmentation and malignancy developing thereon. On the other hand, most of the epitheliomas in xeroderma pigmentosum have been found to be of the basal cell type.

"Biopsy Number 3 from the face presented a picture of an early squamous cell epithelioma in which a secondary infection was superimposed.

"Biopsy Number 4 from the cheek showed a picture of low grade squamous cell epithelioma and of a hemangioma. The vessels were much larger than those seen in granuloma pyogenicum and the epidermal changes were not of the benign type seen in that condition.

"Biopsy Number 5 from the face revealed the histopathologic picture of a nonspecific subacute granuloma. There was an irregular and marked acanthosis of the epidermis but without any evidence of malignant change. In the cutis in many places there was a dense infiltrate composed almost purely of plasma cells. In the neighborhood of a hair follicle a foreign body giant cell reaction was present. In the latter and in other areas a multiplicity of types of cells were seen. There was a very dense amount of melanin pigment in the epidermis in both basal and dendritic cells and chromatophores in the cutis. There were none of the histologic changes seen in xeroderma pigmentosum nor was there much evidence in this section for arsenical pigmentation.

"Biopsies 3, 4 and 5: Studies for arsenic by Osborne's method gave negative results.

"Further sections taken from a pigmented area on the arm removed post mortem showed a histopathologic picture suggestive of arsenical pigmentation and another specimen from the same area showed marked deposits of arsenic trisulphide crystals both in the epidermis and in the cutis as demonstrated by Osborne's technic, but chemical analysis of a piece of skin was negative for arsenic."

Dr. Osborne, at Dr. Montgomery's request, examined his slides, confirmed the presence of arsenic in the skin, and stated that arsenic might be found by his method when direct chemical analysis failed to detect its presence.

COMMENT

The Epitheliomas.—No doubt has been entertained as to the diagnosis of multiple epitheliomas. Clinically, the lesions were typical, and the histopathologic reports positively identified the squamous cell type in repeated biopsies and in sections removed post mortem. In one biopsy specimen the picture simulated that of Bowen's disease.

The child had one white and seven full-blooded Negro great-grandparents. It is possible that even this small admixture of white blood may have been the reason that he lacked the immunity to cutaneous epitheliomas which is common to Negroes entirely of African descent. His normal skin, however, was approximately as black as that of most full-blooded Negroes, and his lack of immunity, if inherited from his white great-grandparent, must therefore be attributed to inherited characteristics other than the amount of pigment in his normal skin. Speculation in regard to the hereditary factors which in this case made the development of epitheliomas possible would be involved in the etiology of cancer; the fact, however, that normal pigment in a black skin did not prevent the occurrence of epitheliomas in this case can be explained on the hypothesis that the Negro as a race owes his immunity not

directly to the color of his skin, but to the protection the pigment affords from such external sources of irritation as exposure to actinic rays. If this view is accepted, it is easily understood that the cutaneous pigment (in this case), however abundant, prevented neither the deposit of arsenic carried by the blood stream, nor its irritant action resulting in the development of epitheliomas.

The Dermatosis.—In regard to the dermatosis to which the epitheliomas were a sequence, a diagnosis of arsenical pigmentation has been made notwithstanding the fact that the distribution was exactly that of xeroderma pigmentosum.

Attempts to evaluate the diagnostic importance of hyperpigmentation and depigmentation and the distribution of these lesions in a Negro should take into consideration the fact that pigmentary changes occur much more commonly in the black than in the white race and are often the sequence of diseases which in a white skin usually are not associated with abnormalities of pigmentation. The greater instability of the pigment of the skin of the Negro is evidenced by the relative frequency of universal leukoderma, the tendency of tinea versicolor to depigment the affected areas, and the frequency with which pigmentation follows exposures to even small doses of roentgen rays in mulattoes. Following scabies in Negroes there often remain small pigmented lesions on the trunk which in many respects are not unlike macular syphilids. In arsenical dermatitis following the intravenous administration of arsenic, a common occurrence is a pronounced pigmentation of the vermilion border of the lips. Furthermore, senile keratoses are extremely rare in Negroes of the darkest complexion, and vascular nevi, if they exist, escape detection. Pigmented nevi are not uncommon in mulattoes, and in the mouths of many Negroes the pigment is unevenly distributed, appearing in large or small patches markedly in contrast to the normal color of the mucous membrane. These patches are of permanent duration and are probably congenital. It may also be noted that dermatosis papillaris nigra occurs only in Negroes.

On account, therefore, of his greater racial pigmentary instability, the distribution of the pigmentary dermatosis in our patient should not be regarded as of as much diagnostic importance as would be attached to such a distribution in a white person.

Xeroderma Pigmentosum.—A preconceived idea entertained by us, that, because of the greater protection against sensitization to light afforded by the pigment layer of the skin, the incidence of xeroderma pigmentosum is less in dark-skinned persons and races was not confirmed by reference to textbooks or to forty-three articles reporting seventy-two cases. No mention of the color of the skin was made in fifty-nine case reports, and in the majority of these the race, when

given, implied a dark rather than a fair skin. The thirteen cases in which the color of the skin was mentioned occurred in the white race, and one patient was described as extremely blond, five as blond, two as having light brown hair, one as a brunette, two as dark and two as very dark. In addition to the cases reported in these articles, eighteen cases were reported from Tunis—the majority of the patients were natives—and thirty-five cases from Japan.

The fact that the patient whose case is reported was a Negro therefore cannot be taken as strong evidence against the diagnosis of xeroderma pigmentosum, even though one might be surprised at the occurrence of a phenomenon of sensitization to light in an almost coal-black skin.

The pigmentary dermatosis in the case reported was in exact conformity in its distribution with that of xeroderma pigmentosum, and all of the lesions also resembled those of that disease, but no telangiectases were found macroscopically or microscopically. It is true that enlarged blood vessels might have been present and yet not visible to the naked eye because of the dark color of the Negro's skin, but failure to detect telangiectases in microscopic studies is definite evidence that such a condition did not exist. It is also true that in the depigmented areas dilated blood vessels would have been conspicuous. The absence of telangiectases is evidence against the diagnosis of xeroderma pigmentosum unless their absence can be regarded as due to a peculiarity common to the skin of all Negroes.

Some observations are being made in an attempt to determine whether telangiectases ever occur in the Negro, or whether in the event of their occurrence their visibility to the naked eye is obscured by overlying pigment. The result of these observations up to the present time indicates that if telangiectases do occur, their occurrence is much rarer in the black than in the white race. Examination of a number of Negroes with diseases of the skin which had caused disappearance of pigment and in which dilated blood vessels usually are seen in the white race disclosed but few and comparatively insignificant telangiectases. The absence of these was notable in cases of leprosy of the skin in Negroes, while in parallel cases in white patients telangiectases were found in almost every case. In leprous nodules, enlarged and superficial blood vessels are frequently seen in white patients; if present in Negroes, they should be visible because of the thinning of the epidermal layer in these lesions, which thinning, Dr. Denney has observed, exists to such a marked degree that it is difficult to distinguish histologically the nodules of a white from those of a black skin. In several advanced cases of erythematous lupus in Negroes, though there had been destruction of the pigment layer, no telangiectases could be found. Similar observations were made with the same negative results

in a few cases of blastomycosis. The absence of telangiectases in the case reported might therefore be attributed to a peculiarity of the Negro skin and not be considered of diagnostic importance.

Xeroderma pigmentosum was excluded as the diagnosis not only because of the absence of telangiectases but also because of the histopathologic picture.

Arsenical Pigmentation.—Though no arsenic was administered for medicinal purposes in the case here reported, it is apparent from the history that arsenic might have been ingested accidentally or possibly inhaled. The strongest evidence in favor of arsenical pigmentation and against xeroderma pigmentosum lies in the histopathologic picture and the presence of crystals of arsenic in the skin. It should be stated that before Dr. Montgomery's microscopic investigations the case was regarded as one of xeroderma pigmentosum, atypical in some of its aspects because of its occurrence in a Negro. Although the photographic appearance of the lesions in our patient closely resembles that in Fordyce and MacKee's case of arsenical pigmentation, the distribution of the lesions in the two cases was quite different. The covered surfaces in our case were practically free, while in that of Fordyce and MacKee the trunk was markedly involved. It is possible that in our patient frequent and prolonged exposure to sunlight may have been responsible for the deposit of arsenic in the skin in the regions which were most subjected to actinic stimulation.

The occurrence of lesions on the palms in our case is more suggestive of arsenical pigmentation than of xeroderma pigmentosum. Squamous cell epitheliomas and epitheliomas simulating Bowen's type are also more in conformity with what would be expected as a sequence of arsenical pigmentation than of xeroderma pigmentosum. A notable but unexplained fact is that the squamous cell epitheliomas, notwithstanding their extreme malignancy, did not metastasize.

CONCLUSIONS

Notwithstanding the rarity with which cutaneous epitheliomas occur in Negroes, the diagnosis made clinically and histopathologically in the case described in this report is that of multiple squamous cell epitheliomas of the face in a Negro boy.

A more generalized dermatosis is diagnosed as arsenical pigmentation on the evidence of the histopathologic picture and on the presence in the skin of arsenic trisulphide crystals. The distribution of lesions, however, was in conformity with that of xeroderma pigmentosum.

The epitheliomas of the face were a sequence of the arsenical pigmentation in this region and, it is assumed, were caused by deposits of arsenic.

The fact that arsenic presumably carried by the blood stream to the skin and there deposited resulted in this case in the development of epitheliomas suggests the possibility that Negro racial immunity to cutaneous epitheliomas is due to protection from external and not from internal sources of irritation, and that the major rôle played by the pigment of the black skin, so far as immunity against epitheliomas is concerned, must be protection against actinic rays and similar natural external sources of irritation.

ABSTRACT OF DISCUSSION

Dr. Howard Fox, New York: I wish to say a few words about the rarity of epithelioma in the Negro skin. In an experience of fourteen years in the Harlem Hospital in New York City, I have never seen an epithelioma of the face in a full-blooded Negro. I have seen this disease on the prepuce and occasionally in the mouth, but never on the face. In the records of three hundred and seventy-four consecutive cases of cutaneous epithelioma in our clinic at the New York University, there was one case of prickle cell epithelioma, but this patient was a mulatto. At my request Dr. Irgang looked over five thousand consecutive case records at the Harlem Hospital, where the patients are nearly all Negroes. He found only one case of basal cell epithelioma of the nose; the patient was a mulatto.

Several years ago in Haiti one of the United States Naval officers told me that he had seen three cases of epithelioma of the skin in full-blooded natives, and that he had confirmed the diagnosis microscopically.

The nearest I have come to seeing epithelioma of the face of an apparently full-blooded Negro was during a visit to Brazil. I photographed a middle-aged man who presented the clinical appearance of epithelioma of the lip and cheek, but no microscopic examination was performed.

Dr. Clark W. Finnerud, Chicago: We see quite a number of Negro patients at the Cook County Hospital and Rush Medical College, and although we have seen no case comparable to the one described by Dr. Hopkins, we have had two instances of epithelioma of the nose, both in persons we took to be full-blooded Negroes. They were both very dark skinned. In both cases we have histologic verification, and in one instance a photograph. I sent the photograph and histologic section of one of these cases to Dr. Hopkins. Perhaps Dr. Senear, if he is present, can tell us of a case seen recently at the Medical School of the University of Illinois, that of a full-blooded Negro with a squamous cell epithelioma of the back of the neck. Recently one of his associates informed me about that case.

An interesting thing about the two cases we saw and from which we took sections was the fact that the lesions dated back to youth, in one case to 5 years of age. The other patient, who was about 65 years old, did not know when the lesion first appeared, but he said that it had been present for at least fifty years. I wonder, because of certain points brought out by Dr. Hopkins, whether it is possible that in his case as well as in these two there may not be something of nevoid character that tends to explain the growths.

Dr. Earl D. Osborne, Buffalo: I wish to say something about the finding of arsenic in tissue. Dr. Hopkins pointed out that arsenic could not be found by chemical examination of a small piece of skin. This is entirely comparable to

the finding of arsenic by microchemical means in the tissue. In the first place, the amount of arsenic in a small section of skin must be almost infinitesimal, and in the process of the destruction of the organic material some of this arsenic is lost. The remainder is too small to be detected by even the most delicate chemical tests. We have demonstrated this repeatedly in our own laboratory.

It should be made perfectly clear that the finding of arsenic in the urine or in the skin of a patient suffering from any lesion of the skin does not necessarily prove that that lesion is due to the presence of arsenic. A very large percentage of our population has taken arsenic at some time in the past, and it may remain in the skin for many years, even as long as twenty or thirty, after its administration. We have had a number of cases of psoriasis in which multiple epitheliomas developed. We have not reported our arsenical findings in these cases because, up to the present time, we have found arsenic absent in approximately the same number in which arsenic was found. Whether the development of epitheliomas in psoriatic lesions is the result of arsenic alone is questionable.

In Dr. Hopkins' case, the boy had keratotic lesions, and epitheliomas developed because of the keratotic lesions, and not necessarily because of the arsenic. We all know about the tendency of all keratotic lesions to degenerate into epithelioma. Dr. Hopkins was kind enough to send me a few sections that Dr. Montgomery had prepared for the finding of arsenic. There is no question but that there is a small amount of arsenic in the skin. As I have pointed out before, there is a difference in the localization of the arsenic following the administration of trivalent and pentavalent arsenic. Following the administration of trivalent arsenic, such as arsphenamine, the largest amount of arsenic is found in the corium around the blood vessel structure, and a relatively small amount in the epithelium. Following the administration of pentavalent arsenic, such as solution of potassium arsenite, the largest amount of the arsenic is found in the epithelium and in the corium immediately below the epithelium and in the sweat and sebaceous ducts.

Dr. Bedford Shelmire, Dallas, Texas: In Texas, where the incidence of cutaneous malignant conditions is extremely high, epitheliomas are rarely observed in the colored race. While this condition is occasionally seen in the lighter colored quadroons and octoroons, I have never observed such a lesion on the normally pigmented skin of a full-blooded Negro. Of the two cases of epitheliomas in full-blooded Negroes which have been recorded in Baylor Clinic, one developed on an old scar on the leg where the skin was partially depigmented; the other developed in the center of a large leukodermic area. The dark pigment of the Negro is apparently a definite protection against the formation of precancerous and epitheliomatous growths.

Dr. Samuel Ayres, Jr., Los Angeles: The discussion of the possibility that arsenic produces the multiple epitheliomas in these cases has been stimulating. I have been interested in this subject as my associate, Dr. Anderson, has made rather a hobby of epitheliomas. I admit that the evidence is rather inadequate and that we should be careful about drawing final conclusions, and yet we have encountered large numbers of ordinary basal epitheliomas and multiple superficial epitheliomas in which the evidence was in favor of arsenic as a causative agent. There was a frequent occurrence of arsenical keratoses of the palms and soles and arsenic was demonstrated by microchemical stains in the tissues of three or four cases that were studied. Pathologic amounts of arsenic were also found in the urine in many of the cases, and a history of definite exposure to arsenic was obtained in some cases. Several cases followed psoriasis, for which the patients had taken solution of potassium arsenite over a period of years, and other cases

occurred in men who had worked in mines or as smelters and were subject to arsenic vapor for a number of years. Since we have been "arsenic conscious" and have examined all cases of epithelioma for arsenical keratoses, we have been impressed by the frequency of their occurrence. We had one patient who took arsenic for several years; he had Bowen's disease on the foot, several benign epitheliomas on the trunk, punctate keratoses on the palms and soles and a cutaneous horn on the trunk.

DR. ELMORE B. TAUBER, Cincinnati: We see a large preponderance of Negroes in our clinic, and I wish to substantiate what Dr. Shelmire said. I do not think that epitheliomas occur in the Negro without a definite underlying cause. We see many Negroes who have keloids and wish to have them removed. Some of these patients have been treated with radium, and all of them have telangiectasis. I think that this substantiates Dr. Hopkins' idea of not finding arsenical depigmentation.

DR. RALPH HOPKINS, New Orleans: I wish to say a word about full-blooded Negroes. A Negro's genealogy is one of the most uncertain points in his history. It often happens that they do not know their ancestry, or it may be that they think they know it but are mistaken.

STREPTOCOCCIC HYPERTROPHIC GINGIVITIS

ARTHUR R. WOODBURNE, M.D.
AND
PHIL NORTHROP, M.S., D.D.S.
GRAND RAPIDS, MICH.

A thorough study of the literature of the past twenty years dealing with hypertrophic gingival lesions shows few reports and these have been largely in the European literature. With the exception of articles by Mead [1] and Keilty,[2] they have dealt almost exclusively with hypertrophy, epuli and other fibromatous growths due to various endocrine and mechanical disturbances such as: those during pregnancy (Monash [3]), those during puberty (Tempestini [4]) and those due to endocrine changes. Hirschfeld,[5] in this country, has written an extensive review of mechanical and irritative factors in the production of gingival hypertrophy and has briefly described an infectious type.

It has been our privilege to see three cases of infection of the gums with the symptoms of an acute infectious disease. These were witnessed during the six months previous to this writing and consisted of a subacute case and two acute cases. It is our opinion that cases of this nature occur much more frequently than one would expect from the literature, and therefore a short article bringing it to the attention of the medical profession at this time is warranted. Mead [1] has reviewed this subject for the dental profession, but so far as we have been able to find there have been no reports in the medical literature.

REPORT OF CASES

CASE 1.—Miss L. H., aged 27, who was referred to the department of oral surgery, gave a history of an acute sore mouth and throat, beginning shortly after her teeth had been cleaned by her dentist six weeks previously. Following this,

---

From the Department of Oral Surgery and Dermatology, the Grand Rapids Clinic.

1. Mead, S. V.: Streptococcic Stomatitis, Internat. J. Orthodontia **18**:748 (July) 1932.

2. Keilty, R. A.: Gingivitis, An Entity Including All Forms from Acute Vincent's to Chronic Pyorrhea, Descriptive Bacteriology, and Pathology, South. M. J. **24**:386 (May) 1931.

3. Monash, S. B.: Proliferative Gingivitis of Pregnancy, Arch. Dermat. & Syph. **24**:580 (Oct.) 1931.

4. Tempestini, O.: Hypertrophic Gingivitis from Humoral Disequilibrium in the Early Appearance of Puberty, Stomatol. **30**:723 (Aug.) 1932.

5. Hirschfeld, Isador: Hypertrophic Gingivitis: Its Clinical Aspect, J. Am. Dent. A. **19**:799 (May) 1932.

her gums became sore, swollen and tender. The soreness extended onto the mucous membrane of the mouth and hard palate. There was some elevation of temperature. Her dentist treated the condition as Vincent's angina with the usual medication used in this disease, including one intravenous injection of neoarsphenamine, with no great relief. Astringent mouth washes produced some temporary improvement, but a few days later there was a marked recurrence, and it was at this time that we saw the patient.

She presented bright red, rolled, soft gingival margins. The border was edematous and pushed up between and along the labial and lingual surfaces of all the incisor teeth, but occupied only the buccal surfaces of the molars. From between the teeth varying sized hypertrophic masses of gum tissues protruded. The larger masses were raised away from the crowns of the teeth in several spaces. No ulcerations, erosions, pustules or vesicles were seen. There was no membrane or purulent discharge. There was considerable salivation, and the patient complained of a sticky secretion in the mouth, which was probably a serous exudate.

Complete physical examination gave negative results except for a pulse rate of 84, a temperature of 99.2 F., the aforementioned condition of the mouth and chronic tonsillitis. The Kahn test was negative. The blood count showed normal white cell and differential counts, with a red cell count of 3,860,000. The urine was normal.

Direct smears taken from the crest of the gums showed many cocci, a few long rods and a few large spirochetes and spirilla.

Dark-field examination showed only rare, coarse spirochetes.

Culture after seventy-two hours showed rare colonies of Staphylococcus aureus, but the plate was largely covered by colonies of Streptococcus viridans. Cultures on Sabouraud's medium showed no fungus growth.

Treatment consisted of frequent washing of the mouth with saline solution. Mercurochrome 2 per cent, as advocated by Mead,[1] was first painted on and injected under the gums; later 1 : 500 solution of metaphen was used. The results from the latter treatment seemed to be better than those obtained with mercurochrome. Hydrogen dioxide in dilute solution was used for a few days as a mouth wash. The hypertrophic tissue was touched up with a saturated solution of copper sulphate occasionally. Inside of one week the mouth was entirely well. There was a slight recurrence in the right cuspid area after two weeks which disappeared in three days when the foregoing treatment was resumed.

CASE 2.—A girl, aged 3, became suddenly ill with diarrhea, fever, general malaise and marked redness and swelling of the gums. The gums presented the same picture of hypertrophy, edema, redness without ulceration, membrane or erosion as in case 1. There was some redness of the throat and tongue. Complete physical examination gave negative results, except for the condition of the mouth, a pulse rate of 110 and a temperature of 101.2 F.

The mouth was washed with a solution of hydrogen dioxide three times a day, and the gums irrigated with metaphen; a saline mouth wash was used frequently.

There was a rapid response, and the mouth was entirely well in six days. There was no recurrence.

CASE 3.—A. W., aged 32, the father of the patient in case 2, became suddenly ill four days after the onset of the condition in the daughter. He had diarrhea, headache, general malaise, fever and anorexia, followed in twenty-four hours by rapid hypertrophy of the gums, a sticky, stringy saliva and marked pain and tenderness of all gum tissue.

Compound solution of potassium arsenite as a mouth wash gave no results after two days, and the patient was seen at this time. The condition of the mouth was identical with that in case 2. General examination gave negative results, except for a pulse rate of 94 and temperature of 100 F.

The treatment was the same as that in case 2, except that cauterization of the hypertrophic tissue with saturated solution of copper sulphate and 7 per cent chromic acid was tried, which therapy seemed to make the condition worse; ultraviolet radiation applied through a quartz rod also gave no definite improvement. Salicylates and alkalis internally gave considerable relief from the toxic manifestations. The gums became normal in about ten days, and there was no recurrence.

COMMENT

Streptococcic hypertrophic gingivitis must surely be more common than one would expect from a review of the literature, since we have seen three cases within a period of three months. The differential diagnosis from the more chronic forms due to endocrine changes,

Model made in composite to bring out more clearly the characteristics of streptococcic hypertrophic gingivitis.

trauma or Vincent's infection should offer no difficulty when the major characteristics of this acute infection are kept in mind.

Hirschfeld,[5] in an extensive article on hypertrophic gingivitis, gave a review of the factors of malocclusion, torsion and crowns as an etiologic factor in the chronic cases. The case which he described as hypertrophy due to an atypical Vincent's infection might well have been a subacute streptococcic hypertrophic gingivitis since he did not mention the loss of tissue which is usually characteristic of a Vincent's infection. He classified it as Vincent's disease because it cleared up under mild antiseptic medication, "with the rapidity characteristic of a Vincent's infection." It has been our experience that cases of streptococcic hypertrophic gingivitis respond in about one week which is the usual period required in a Vincent's infection.

The differentiation from the chronic forms due to endocrine changes; mouth breathing, malocclusion, torsion, overhanging crowns, cavities, calculus and other irritating substances; scurvy, heavy metal poisonings and leukemia is easily made from the history of an acute onset with malaise and fever as in an acute infection, the presence of Strepto-

coccus viridans in almost pure culture and the rapid response to gentle antiseptic medication.

Microscopic examination in cases of Vincent's angina will show the usual numerous large spirochetes and fusiform bacilli, while in streptococcic hypertrophic gingivitis these are extremely rare and culture will yield the characteristic organism, Streptococcus viridans.

Treatment beside the mild antiseptic medication as recommended should include, after the acute symptoms have subsided, a rigid oral prophylaxis and the elimination of all irritating factors, such as abscessed teeth, irritating crowns and fillings and the removal of partially impacted teeth, all of which may keep the resistance of the tissue lowered as well as retain the infective organisms which under proper conditions are apt to cause a recurrence of the infection or prevent a complete recovery. It is desirable that all other possible foci should be investigated and eliminated.

Strong antiseptic and caustic or stimulating medication, such as copper sulphate, chromic acid and ultraviolet rays, which are frequently used in the Vincent's infection, seem to be definitely contraindicated in the treatment of this condition since our patients became worse after their use. We conclude, therefore, that one should attempt to prevent further damage by the organisms to the tissues and to destroy all possible organisms without damaging the resistance of the tissue, and that this should be done by conservative mild treatment. The internal medication in use in other acute infectious diseases seems to make the patient more comfortable and to shorten the course of the disease.

The following plan of topical medication has given the best results in our hands. When the patient is first seen the mouth is irrigated, not sprayed, as the air pressure seems to injure the acutely sensitive mucous membrane at this stage, with either a dilute solution of potassium permanganate or a solution of hydrogen dioxide. After the mouth is packed with gauze, a 1 : 500 solution of metaphen is applied with a small wire loop and is carried beneath the hypertrophic tissue along the side of the tooth. It is our belief that probably it is the thoroughness of the work which is most important. At first this treatment should be done twice daily. The patient is instructed to irrigate the mouth every hour, alternating with potassium permanganate, 1 : 5,000, and hydrogen dioxide, 1.5 per cent solution. After the acute condition subsides, the teeth should be scaled carefully.

Streptococcic hypertrophic gingivitis, we believe, is an acute infectious disease. It is probably contagious, in view of the fact that the disease developed in the father (case 3) of one of the patients (case 2) four days after the onset in case 2, with the same symptoms and signs and following an incubation period which is frequent in acute streptococcic infection.

SUMMARY

1. An acute infectious disease, due apparently to Streptococcus viridans, which is characterized by an acute inflammatory process of the gums with marked hypertrophy is here described.

2. This infection seems to be a definite entity which should be differentiated from other acute and chronic infections and endocrine and mechanical disturbances of the gingiva.

3. The treatment should be that of an acute systemic infection plus mild antiseptic local medication.

Obituaries

EARL DEAN CRUTCHFIELD, M.D.
1890-1933

American dermatologists learned with sorrow of the death of Dr. Crutchfield on Nov. 30, 1933. He was born in New Mexico on March 7, 1890, but from infancy his life was spent in Texas. He obtained his bachelor's degree in Southwestern University, Texas, in 1911; taught school for four years, a training and education that seem so valuable to many men, and then entered the medical department of the University of Texas in 1914, from which he graduated with a brilliant record in 1918. After an internship, he studied dermatology at the Vanderbilt Clinic, New York, and under Dr. George MacKee. He began the practice of dermatology at Galveston and became professor of dermatology in the University of Texas, retaining that chair until he moved to San Antonio in 1927. After that he practiced in San Antonio until his death.

His interest in dermatology was intense and he made frequent contributions to the subject. These contributions showed a real capacity for research. His exhaustive memoir (with Boyd) on mycetoma is an outstanding contribution, and his note on dermatitis due to the Portuguese man-o-war is a permanent addition to the knowledge of that subject. Every American dermatologic text contains references to Dr. Crutchfield's works on these subjects and others. He was an excellent teacher and popular with undergraduate students. He had the rare quality of stimulating in other men interest in his field and he has to his credit a number of disciples who are dermatologists of ability. He was a handsome, friendly and cultured man and he had a fine personality. He leaves many friends who mourn his premature death.

Abstracts from Current Literature

AGRANULOCYTOSIS IN CHILDHOOD. THURMAN B. GIVAN and BENJAMIN SHAPIRO, Am. J. Dis. Child. **46**:550 (Sept.) 1933.

In reviewing the literature on agranulocytosis in childhood and reporting a case of the same condition, Givan and Shapiro point out that in the thirty reported cases all the patients except four had definite histories of immediately antecedent acute infections. Twenty-six of the thirty patients died. The authors' patient was treated with adenine sulphate given intravenously, with good results. Neoarsphenamine was given late to clear up the superficial oral infection. Later the patient withstood two radical operations on the jaw, and up to ten months later there had been no recurrence.

CARCINOMA OF THE SKIN IN CHILDHOOD. JAMES R. LISA, Am. J. Dis. Child. **46**:561 (Sept.) 1933.

Lisa briefly reviews the reported cases of carcinoma of the skin in childhood, eleven of sixteen cases of which developed on the basis of xeroderma pigmentosum. He then reports a case which he apparently considers an epithelioma of the lip in a boy aged 10 years, but which more likely was a granuloma pyogenicum.

TREATMENT OF CONGENITAL SYPHILIS WITH ACETARSONE (STOVARSOL) BY MOUTH. ALFRED S. TRAISMAN, Am. J. Dis. Child. **46**:1027 (Nov.) 1933.

Acetarsone by mouth was used in the treatment of fifty-four patients with congenital syphilis. The first week the dosage was 0.005 Gm. daily per kilogram of body weight; the second week, 0.010 Gm.; the third week, 0.015 Gm., and the fourth week, 0.020 Gm. For the following five weeks the dosage was kept at 0.020 Gm. daily per kilogram of body weight. The duration of the course of treatment was nine weeks. A rest of six weeks followed a course of treatment.

In the group of infants under 1 year of age 71 per cent showed a reversal of the Wassermann and Kahn reactions. In the group of children between the ages of 1 and 6 years, the Wassermann reaction became negative in 55 per cent and the Kahn reaction in 33 per cent. In the group between 6 and 12 years of age, the Wassermann reaction became negative in 47 and the Kahn reaction in 19 per cent.

Forty patients completed a second course of acetarsone therapy; the Wassermann reaction became negative in 50 per cent and the Kahn reaction in 33 per cent.

The clinical condition improved rapidly, and the physical development also showed marked improvement.

ACRODYNIA. CLEMENT COBB, Am. J. Dis. Child. **46**:1076 (Nov.) 1933.

The article contains a review of the subject of acrodynia and a report of four additional cases with special consideration of the roentgenologic observations in the bones of the extremities. There is a good résumé regarding the etiology, pathology, symptoms and diagnosis.

ANDERSON, Los Angeles.

THE ETIOLOGIC RELATIONSHIP OF SEVERE ALCOHOLISM TO PELLAGRA. T. D. SPIES and H. F. DE WOLF, Am. J. M. Sc. **186**:521 (Oct.) 1933.

Spies and De Wolf believe that pellagra following severe alcoholism should be regarded as the same condition as endemic pellagra without alcoholism. They base their contention on the fact that both conditions are characterized by the same dietary insufficiency, the same seasonal occurrence and the same lesions and symptoms.

Ten patients with alcoholic pellagra were given a well balanced diet together with 75 Gm. of autoclaved yeast and from 600 to 900 cc. of whisky. They recovered with no apparent ill effects in spite of the liberal allowance of whisky.

The authors think that the alcoholic factor becomes operative by decreasing the appetite and thus making the diet inadequate to prevent pellagrous lesions.

EXPERIMENTAL REPRODUCTION OF LIPEMIA. A. C. CURTIS, J. M. SHELDON and H. C. ECKSTEIN, Am. J. M. Sc. **186**:548 (Oct.) 1933.

In a case of severe diabetes with lipemia, lipemia and lipemia retinalis were reproduced experimentally. The lesions of xanthoma diabeticorum were found to disappear when the fat in the blood approached normal limits, but the lesions did not reappear after experimental lipemia was induced, although the time of the induced lipemia may have been too short.

JAMIESON, Detroit.

TREATMENT OF CANCEROUS OR POTENTIALLY CANCEROUS CERVICAL LYMPH-NODES. VILRAY PAPIN BLAIR and JAMES BARRETT BROWN, Ann. Surg. **98**: 650 (Oct.) 1933.

The authors' conclusions are based on the results of treatment in 473 cases of squamous cell carcinoma or adenocarcinoma arising above the body of the mandible. In all cases in which squamous cell cancer is present on the lip or within the mouth or pharynx below the level of the oral slit, an attempt is made to eliminate the possibly infected glands without waiting for evidence of metastasis. The primary growth is controlled first, and radiation is directed to the glands of the neck while awaiting a favorable opportunity for radical treatment of the glands. Combined operation may at times be necessary, but it gives a higher rate of mortality. Neither in their own experiences nor in the literature have the authors found a method for dealing with metastases superior to block surgical dissection. Such dissection is not feasible if the carotid artery is involved, but an ingenious method of irradiating the mestastases in that event is described. The tissues are exposed by retracting the overlying dermal flaps and radiation (either intensive roentgen rays or radium) is directly applied. Blair and Brown believe that if roentgen irradiation is ever to displace removal in the treatment of cancerous cervical nodes such direct exposure will, at least for a time, be one of the steps in the development of the process.

INJURY AS A CAUSATIVE FACTOR IN THE DEVELOPMENT OF MALIGNANT TUMORS. WILLIAM B. COLEY and NORMAN L. HIGINBOTHAM, Ann. Surg. **98**:991 (Dec.) 1933.

Coley and Higinbotham review the literature concerning the more important medical and medicolegal aspects of the causal relationship between trauma and malignant growths and from this review and their own experience they draw the following conclusions: A single local trauma may be an important factor, probably the determining factor, in the development of a malignant tumor of any type. Trauma is a causative factor in a larger proportion of sarcomas than of carcinomas, and in a larger proportion of sarcomas of the bone than of those of the soft tissues. The time elapsing between the injury and the appearance of the tumor is often much shorter than is recognized by most writers. While courts and compensation bureaus here and abroad have generally recognized the single trauma as a competent producing cause of all types of malignant tumor, it is only fair to the insurance companies to study each case and to judge it on its own merits. If the case considered fulfils all the conditions laid down by Legond, a causal relationship between the injury and the tumor must be admitted.

PRURITUS ANI: ITS ETIOLOGY AND TREATMENT. ROBERT A. SCARBOROUGH, Ann. Surg. **98**:1039 (Dec.) 1933.

After a brief survey of the literature on the causes and treatment of pruritus ani, Scarborough discards all etiologic theories other than that of abnormal anal

conditions, the most important of which is interference with proper closure of the upper level of the anal canal, thereby enabling irritating rectal secretions to seep into the anus, whose stratified but noncornified epithelium is peculiarly susceptible to maceration, erosion and fissuring, with consequent irritation of the underlying nerve bulbs. A relaxed sphincter, hemorrhoids or hypertrophied papillae may interfere with such closure; cryptitis and foreign bodies may result in irritating discharges. Fungous infections are discounted except as being secondary. Of 304 patients who came to Scarborough's proctologic clinic, 152 suffered from pruritus ani. A definite local cause of the type mentioned was found in every case in which an examination was made except the first one. Because of the expense involved in surgical treatment only 63 of the 152 submitted to the necessary therapeutic measures. Fifty-two of the latter group completed the necessary surgical measures with "complete and absolute relief from their pruritus, without recurrence, and without the use of analgesic ointments or the employment of the various nerve-cutting or nerve-blocking measures which may give temporary relief."

WIEDER, Milwaukee.

HUMAN CAPILLARIES IN HEALTH AND DISEASE. I. S. WRIGHT and A. W. DURYEE, Arch. Int. Med. **52**:545 (Oct.) 1933.

Among other conditions studied was scleroderma. It was found rather difficult to investigate the capillaries in persons with scleroderma. In this disease the vessels usually appear irregular and distorted; the blood flows slowly and stops when the local or body temperature is lowered. With elevation of the temperature the flow quickens and the blood becomes brighter red.

In Raynaud's disease the capillaries are long, dilated, characteristically atonic loops. The blood flows slowly, and the capillary response to changes in temperature is marked.

Capillary changes in thrombo-angiitis obliterans are classified in two groups. In the group without vasoconstrictor phenomena the capillaries are moderately dilated with an increase in the active open ones. The flow of the blood is slow. The group with vasoconstriçtor phenomena shows a marked capillary constriction at room temperature or lower. The blood flows slowly and the patient becomes cyanotic.

In erythromelalgia the capillary loops may be irregular, gigantic and grotesque with a sluggish flow of blood, which may even form stagnant pools at the ends of the capillaries.

Capillary permeability was found to be normal in five of eight cases of mesodermal syphilis but was increased in three cases with meningeal involvement.

JAMIESON, Detroit.

METHODS FOR MICROCHEMICAL DEMONSTRATION OF ARSENIC IN TISSUES. H. TANNENHOLZ and K. B. MUIR, Arch. Path. **15**:789 (June) 1933.

A series of carefully controlled experiments casts doubt on the specificity of the microchemical test for arsenic in the tissues which was introduced by Justus and modified by Brünauer and by Osborne. Sections of tissue fixed in formaldehyde and treated with hydrogen sulphide showed in normal controls crystals that were identical with those seen in sections from tissues containing arsenic. These crystals were not soluble in carbon disulphide, which proved that they were not sulphur, and they did not dissolve in sodium hydroxide, so that they evidently were not arsenic trisulphide as had been supposed. Identical crystals were produced by similar treatment of egg albumin alone, egg albumin containing sodium arsenite or red blood cells or blood serum, an exsanguinated rat heart and a heart containing blood. Crystals were not produced when the tissue was fixed in alcohol before treatment with hydrogen sulphide nor when the tissue was treated with hydrogen sulphide in an acid medium before fixation; but in both these experiments normal

sections were identical with those containing arsenic. The authors believe that the crystals are a combination of sulphur and protein rather than crystals of arsenic trisulphide.

CARO, Chicago.

PERSISTENCE OF IMMUNITY AFTER THE ABOLITION OF ALLERGY BY DESENSITIZATION. ARNOLD R. RICH, FREDERICK B. JENNINGS, JR., and LILLIAN M. DOWNING, Bull. Johns Hopkins Hosp. **53**:172 (Oct.) 1933.

In a series of experiments with rabbits Rich and his co-workers attempted to determine whether immunity to infection with pneumococcus and Pasteurella aviseptica would be less efficient after the abolition of allergy by desensitization. They found that "when the capacity for reacting with allergic inflammation is completely destroyed by the injection of large doses of killed bacteria into the veins of hypersensitive, immune animals, immunity to intracutaneous infection with millions of lethal doses of living, virulent bacteria remains intact. Inflammation at the site of infection in such animals is far less in amount than in untreated allergic, immune animals—far less, indeed, than in normal controls, but the bacteria are prevented from spreading from the site, and are as effectively destroyed as they are in the allergic, immune body. The immune state acts to enhance so greatly the protective power of the inflammatory mechanism that much less, rather than much more, inflammation is required to protect the body from infection. Damage to tissue at the site of infection is also far less in the desensitized animals than in the allergic ones.

"Even in the highly allergic immune body, therefore, allergic inflammation is not necessary for protection against infection, and in its absence the body is protected with much less damage to tissue than that which occurs in the allergic body."

ANDERSON, Los Angeles.

CONGENITAL NEUROFIBROMATOUS MACROGLOSSIA. H. MÜLLER, Centralbl. f. allg. Path. u. path. Anat. **57**:55, 1933.

This rare condition was found in a boy aged 6 years who was mentally retarded. Over the entire body there were numerous nevi, some finely and some coarsely pigmented. There was also a tumor of the right side of the dorsal third of the tongue. The papillae of the tongue were enlarged, and scattered in the muscle were pinhead-sized nodules and strands of gray-yellow tissue. The nodules contained medullated nerves in their central parts but no ganglion cells. The muscle about them was loose.

RUKSTINAT. [ARCH. PATH.]

RELATION BETWEEN AN ACID OR AN ALKALINE DIET AND IMMUNITY: A. M. BONANNO, Ztschr. f. Immunitätsforsch. u. exper. Therap. **77**:19, 1932.

The acid-base equilibrium of rabbits and guinea-pigs was changed by feeding them with calcium and ammonium chloride, with sodium bicarbonate and with sodium citrate. An acid diet was followed by a decrease in the bactericidal and complementary qualities of the blood. A change in the normal albumin-globulin ratio in the blood was noted, there being a rise in albumin and a drop in globulin. An alkaline diet was without effect. An acid diet impaired the ability to produce immune agglutinins and to resist infection and increased the severity of anaphylactic reactions. A modification of the diet in either an acid or an alkaline reaction led to a marked lowering of resistance to intraperitoneal infection with tubercle bacilli.

APPLICATION OF RECENT PRECIPITATION REACTIONS FOR THE DEMONSTRATION OF SYPHILIS IN RABBITS. F. E. HAAG and W. LEVEN, Ztschr. f. Immunitätsforsch. u. exper. Therap. **77**:25, 1932.

The Kahn test gave uniformly negative results with diluted serums (1 : 10) of normal healthy rabbits. The reactions were positive in a considerable number of cases when undiluted serum was used or when the Kahn citochol or the Meinicke

test was employed. Latent syphilis could not be detected by means of any of these tests. In the presence of an active infection the Kahn citochol test was the only one that produced a considerable number of positive reactions, but in view of the positive results in healthy rabbits no definite conclusions could be drawn. No differences were observed between the serum reactions of animals infected with syphilis and those of rabbits infected with framboesia tropica. The results contradict the report of Taishin Saito *(Ztschr. f. Hyg. u. Infektionskr.* **110**:603, 1929), who claimed to have found in the Kahn test with diluted serum a means of diagnosing syphilis in the rabbit. The Kahn citochol reaction and particularly the second modification of the Mueller "Ballungs" reaction were found very well suited to the diagnosis of syphilis in rabbits, but only after precipitation of globulins in the serum with diluted hydrochloric acid by the method of Sachs and Georgi. Triple and double dilutions had to be employed instead of the original tenfold dilution.

ORAL IMMUNIZATION WITH VIRULENT STAPHYLOCOCCI AND STREPTOCOCCI. HANS WINZELER, Ztschr. f. Immunitätsforsch. u. exper. Therap. **77**:60, 1932.

Guinea-pigs weighing from 230 to 280 Gm. were fed living or killed cultures of highly virulent strains of Staphylococcus aureus or Streptococcus haemolyticus. Some of the animals were treated with ox bile, a sodium salt of a bile acid or sodium benzoate previous to being given the bacterial suspension. When living bacteria were used, active immunity against subsequent parenteral injections of multiple lethal doses of Staph. aureus was obtained in seventeen of twenty-five animals. Dead bacteria only slightly increased the natural resistance. The immunization with streptococci was not successful. The preliminary administration of bile or bile salts was found not necessary.

QUININE AND ULTRAVIOLET RAYS. O. JÍROVEC and V. BOUŠE, Ztschr. f. Immunitätsforsch. u. exper. Therap. **78**:100, 1933.

The toxicity of solutions of quinine, acriflavine, eosin and pyronine for paramecia did not increase following irradiation of the solutions with ultraviolet rays. This contradicts the reports of Roskin and Romanowa, who had observed a marked increase of the toxic effect of quinine on paramecia following irradiation.

COMPARATIVE COMPLEMENT-FIXATION TESTS IN LEPROSY, TUBERCULOSIS AND SYPHILIS. G. KORNEL, Ztschr. f. Immunitätsforsch. u. exper. Therap. **78**:207, 1933.

The technic for the preparation of an antigen from a leproma is described. It was somewhat more specific than various syphilitic antigens and the antigen of Witebsky-Klingenstein-Kuhn, for which a marked specificity in the complement-fixation test for tuberculosis was claimed by its authors. The antigens employed for the serologic diagnosis of syphilis and of tuberculosis did not permit a differentiation of leprosy in the presence of simultaneous tuberculous or syphilitic infections.

COMBINED ACTION OF ARSPHENAMINE AND ULTRAVIOLET RAYS ON SPIROCHAETA PALLIDA. S. S. ORLOW and L. B. LEWINSON, Ztschr. f. Immunitätsforsch. u. exper. Therap. **78**:264, 1933.

Rabbits were given combined treatment with arsphenamine and ultraviolet rays after the development of primary syphilitic lesions. The fur on the abdomen was removed and an erythema dose given (usually from three to five minutes at 25 cm.) immediately after the injection of neoarsphenamine and again on the following day. The result was a marked increase in the therapeutic effect and a shortening of the period of illness. The spirochetes in the primary lesion disappeared earlier than in the controls. The toxic effect of the drug was not increased. Orlow and Lewinson advocate a wider application of the combined treatment in the clinic.

CAUSE OF THE POSITIVE WASSERMANN REACTION IN MALARIA. O. FISCHER and O. D. GÜNSBERGER, Ztschr. f. Immunitätsforsch. u. exper. Therap. **78**:295, 1933.

The occurrence of a positive Wassermann reaction during, and for various lengths of time after, a malarial attack is due, according to Fischer and Günsberger, to the development of antibodies against the lipoids of the destroyed red blood cells. An alcoholic extract of erythrocytes reacted in twenty-one of twenty-eight cases with serums of patients with malaria, occasionally but only in low dilutions with syphilitic serums and not at all with normal Wassermann-negative serums. The differentiation between the serum of patients with malaria and that of patients with syphilis was possible by the evaluation of the titers obtained in complement-fixation tests with various extracts. A highly sensitive extract of beef heart was particularly helpful.

TRANSFERABLE AND INHIBITING SUBSTANCES IN THE BLOOD OF ALLERGIC PATIENTS. W. KREMER, Ztschr. f. Immunitätsforsch. u. exper. Therap. **78**:382, 1933.

The transferable substances (allergens) were determined by means of the method of passive transfer, and the inhibiting substances (antiallergens) were demonstrated by mixing the allergens with the patient's blood or blood serum and then injecting the mixture intracutaneously. The usual cutaneous reaction was inhibited in the presence of antiallergens. Both types of substances are found frequently, but they need not be present simultaneously, as was seen in three patients who had only one kind of substance in the blood. Both types of substances always correspond to the allergens to which the patient is sensitive. They were never found in nonallergic persons. The antiallergens are transferable to the skin of other persons sensitive to the same allergens. The author concludes that the transferable allergens and the antiallergens are not identical. DAVIDSOHN. [ARCH. PATH.]

ECZEMATOUS CHANGES IN THE SKIN AND GASTRIC FUNCTION. ISAM MIAKE, Jap. J. Dermat. & Urol. **34**:345 (Oct.) 1933.

Following a special test meal, the gastric contents of rabbits were tested for acidity every fifteen minutes for two hours using as indicators a 1 per cent solution of alcoholic phenolphthalein and a 0.5 per cent solution of dimethyl-amino-azobenzene. The tests were carried out first on normal animals and then on rabbits with a dermatitis provoked by applications of croton oil. In the earlier stages of the dermatitis, the gastric function was found to be increased in some instances and diminished in others. During the period of healing, the gastric function was always increased, but when the process was completely healed the function returned to normal.

A PREVIOUSLY UNDESCRIBED ANOMALY OF PIGMENTATION: DYSCHROMATOSIS UNIVERSALIS HEREDITARIA. IKUZŌ TŌYAMA, TOKUJI ICHIKAWA and YOSHIO HIRAGA, Jap. J. Dermat. & Urol. **34**:360 (Oct.) 1933.

Except for the greater extent this anomalous condition of the skin resembles the condition described as acropigmentatio by Komaya in 1920, as leukopathia punctata et reticularis by Matsumoto in 1927 and as dyschromatosis symmetrica hereditaria by Tōyama four years ago. In the present cases the condition, which involved the entire bodies of the patients with the exception of the palms and soles, consisted of pigmentary flecks, varying in shape and size from those of a grain of rice to those of a bean but being usually about the size of a pea. The lesions were sharply delimited and thickly set, and the intervening areas of leukoplakia were of like shapes and sizes. The condition was not so pronounced in the younger patients, and different stages of the process could be observed in the group. The hereditary character of the condition was indicated by the fact that in one

family the condition was present in the mother and in both children (males) and that in the other it occurred in the mother and in two (females) of the six children, who were of both sexes.

EXPERIMENTAL STUDY OF THE SENSITIVITY OF THE SKIN TO ULTRA-VIOLET IRRADIATION IN WHITE RATS WITH VITAMIN B DEFICIENCY. SEIZO TSUCHYA, Jap. J. Dermat. & Urol. **34**:384 (Oct.) 1933.

In rats on a normal diet there was little or no change in sensitivity to irradiation during five weeks of observation. In rats with artificially induced deficiency of vitamin B sensitivity, as a rule, had increased by the second week, but by the third week it had begun to decrease and from then on it continued to decrease. By the third day of the period of recovery (induced artificially by brewers' yeast) sensitivity had begun to increase, but by the seventh day rather confusing results had appeared: in some cases hypersensitivity developed, but in others depressed sensitivity was still observable. Chemical analyses of the skin and blood serum were made to determine the values of the calcium and potassium and the ratio of these two metals to each other. Determinations were also made of the nonprotein nitrogen and of the sugar in the skin during fasting. For the controls these values remained practically constant throughout the entire period. In the vitamin B deficient rats the ratio between calcium and potassium began to vary, the calcium rising to almost double its initial value by the fifth week and the potassium sinking to practically one half. A period of recovery of seven days was required to bring these values back to the normal range of variation. The nonprotein nitrogen of both the skin and the blood serum began to rise during the first two weeks of vitamin B deficiency; it remained stationary during the third week and rose slightly again during the fourth week. By the third day of recovery the nonprotein nitrogen of the skin and blood serum had sunk to the lower normal levels, but by the seventh day in both the skin and the blood it had returned to normal. In vitamin B deficiency the values of dermal sugar during fasting had risen noticeably by the second week, and by the end of the fourth week the values for the skin and the blood serum had risen rather high. By the third day of recovery the values for the blood serum had returned to normal but the values for the skin did not become normal until the seventh day.

STUDIES ON SERUM ALBUMIN IN ITS RELATIONS TO DERMATOLOGY (SECOND COMMUNICATION). THE INFLUENCE OF ARSPHENAMINE ON THE SERUM ALBUMIN IN SYPHILIS IN MAN AND IN EXPERIMENTAL RABBITS. T. MURAKAMI, Jap. J. Dermat. & Urol. **34**:464 (Nov.) 1933.

The first communication dealt with the behavior of the serum albumin in syphilis; this report concerns the effect of the injection of a preparation of arsphenamine on the serum protein in syphilitic patients and in syphilitic rabbits. Intravenous injection of the drug causes little change in the total amount of protein or in the albumin-globulin ratio. In healthy rabbits intravenous administration of 1 Gm. per kilogram of body weight produces a moderate lowering of the level of protein. The level, however, returns to normal within twenty-four hours. When the nonsyphilitic rabbit is given subcutaneous injections of solarson, there is a marked lowering of the protein level within three hours, and it lasts over twenty-four hours.

STUDIES ON SERUM ALBUMIN IN ITS RELATIONS TO DERMATOLOGY (THIRD COMMUNICATION). SERUM PROTEINS IN CASES OF BURNS. T. MURAKAMI, Jap. J. Dermat. & Urol. **34**:480 (Nov.) 1933.

Determinations of serum protein were made on four patients, three of whom had second degree burns. The protein content was found somewhat diminished and the globulin fraction increased at the expense of the albumin fraction. In experimental rabbits there was a diminution of protein content following the burn, the duration of the phenomenon depending directly on the extent of surface involved in the burn.

EPITHELIOMA ADENOIDES CYSTICUM, BROOKE. I. EJIRI, Jap. J. Dermat. & Urol. **34**:493 (Nov.) 1933.

Three cases are reported. Heredity was evident in two adult patients, mother and daughter. In these two cases the histologic findings resembled those in the other case in most particulars, but the cells of the epithelial cell masses more nearly resembled cells of sebaceous glands and there were a few areas of calcium deposits. The mother had had the eruption since her twenty-first year and the daughter since her twelfth year. In both the eruption had spread gradually to involve the greater part of the face, being most pronounced toward the median line.

The other case was that of a child aged 2 months. There was an oval plaque on the right cheek, near the ear, consisting of thickly set, partially confluent masses of slightly smooth, glistening, dense nodules, varying in size from that of a hemp seed to that of a pea. They scarcely differed in color from the surrounding skin. Histologically, two types were present in different areas; one resembled basilioma as usually described, with the cyst formation characteristic of epithelioma adenoides cysticum, and the other presented rather the appearance of squamous cell cancer with epithelial pearls.

In the first the epidermis was normal. The cutis showed a network of branching epithelial strands and masses in which were cystic cavities filled with reddish or bluish masses. In other places the cell protoplasm showed a more vacuolated structure, stained poorly and was reminiscent of sebaceous gland cells. There were numerous rudimentary hair follicles, and the number of sebaceous glands was somewhat increased. There was an increase in fibroblasts, as well as moderate lymphocytic infiltration and a few foreign body giant cells.

In the second type the stratum corneum was thickened and scaling. In the rete malpighii there was acanthosis with edematous swelling and occasional formation of vacuoles. In the cutis the epithelial masses consisted of squamous epithelial cells with edematous swelling and occasional formation of vacuoles or cavities filled with horny masses, or structures resembling epithelial pearls. There were a few cell masses resembling hair follicles but none resembling sebaceous cells.

LEUKOMELANODERMA DUE TO INJURY OF THE VEGETATIVE NERVOUS SYSTEM CAUSED BY ARSPHENAMINE MEDICATION. K. KIMURA, Jap. J. Dermat. & Urol. **34**:504 (Nov.) 1933.

A healthy married woman was given injections of a preparation of arsphenamine because of several eruptions of itching papules on the face, flanks and external genitalia, which had disappeared, leaving pigmented flecks. With the seventh injection, some itchy, erythematous papules appeared and remained for about a week. With the ninth injection and henceforth with each succeeding injection the eruption returned and became worse until a diffuse, itchy, reddish, edematous swelling developed over the whole body; fever, chills and general malaise appeared. After several months of treatment by a dermatologist, the eruption gradually disappeared with much desquamation, pigmentation and depigmentation. At present the whole body is irregularly covered with flecks and patches of melanoderma of brownish-gray to brownish-black hue, interspersed with and sometimes appearing within the larger whitish spots and patches of leukoderma. These in many places exhibit a markedly pigmented border. The skin is thickened in places, especially at the folds, and it is hyperkeratotic in the pigmented areas, particularly about the hair follicles, which appear as elevations with grayish-white specks or pityriasis-like scaling on the apexes. The skin is rough and dry. There are no sensory disturbances or other noteworthy evidences of pathologic involvement of the vegetative nervous system.

A CONTRIBUTION TO THE SUBJECT OF EXANTHEMS DUE TO GONOCOCCUS. T. ICHIKAWA and S. OHMORI, Jap. J. Dermat. & Urol. **34**:511 (Nov.) 1933.

This is the first report of the finding of the gonococcus in the cutaneous eruption itself. The case reported is that of a young man with acute gonorrhea. About

the fifteenth day a mildly itching exanthem appeared over the whole body. At the time he visited the urologic clinic, the acute stage of the urethral involvement had largely disappeared, but the entire body, with the exception of the head and face, was thickly covered with patches of erythema, from the size of a pea to that of a hen's egg; in some places these had become exudative. Histologic study of an exudative, erythematous area on the right thigh disclosed a condition resembling the erythematopapular stage of erythema exudativium mulitforme of Hebra. Gonococci were seen in and among the infiltrating cells about the vessels and even in groups within the mildly edematous epidermis. These gonococci were typical in many places and degenerated in others. No cultures of the blood or lesions were carried out. Later the condition entirely disappeared without local treatment. Some convincing photographs of the organisms found in the tissues are given.

BRENNAN, Chicago.

FAMILIAL OCCURRENCE OF LEUKEMIA. SVEND PETRI, Acta path. et microbiol. Scandinav. **10**:330, 1933.

The literature is reviewed and thirty-three cases of familial leukemia are described, in eleven of which the condition was unmistakable. The lymphatic type occurred in twenty-two instances. There was an average of three cases in a family. The author adds a report on chronic lymphatic leukemia in two brothers. There is no evidence of hereditary transmission of leukemia, although some endogenous factor is associated. The presence of infection or of a common external agent could not be ruled out. The possibility of mere coincidence in "familial" leukemia must be considered. Lymphatic leukemia occurred in 85 per cent of related persons, while myelogenous leukemia occurred in nonrelated persons.

KLINE. [ARCH. PATH.]

Society Transactions

SAN FRANCISCO DERMATOLOGICAL ASSOCIATION

May 5, 1933

E. K. STRATTON, M.D., *Chairman*

STEATOCYSTOMA MULTIPLEX. Presented by DR. S. C. WAY.

J. H., aged 24, complains of innumerable nodules within the skin, which vary in size from that of a pinhead to that of a hazelnut and which occur chiefly on the chest, abdomen and buttocks and, to a lesser extent, on the arms and forehead.

The nodules were noticed first three and one-half years ago; since then they have been increasing in number and size. No discomfort is felt except when infection occurs. The skin over the nodules appears to be normal. When a nodule is incised, a yellowish, thick, slightly transparent material can be expressed.

DISCUSSION

DR. J. M. GRAVES: I should like to ask Dr. Way to say something about the treatment of the condition.

DR. S. C. WAY: The only treatment that I know of is to incise each cyst and express the contents. Roentgen therapy may, of course, be considered.

DR. H. E. MILLER: I have seen some cases of this type in private practice and in the clinic. I saw the first one about ten years ago. Some of the lesions were emptied, and an attempt was made to analyze the contents. Fractional roentgen therapy, as used in acne, seemed to be of benefit. The lesions were located almost entirely over the chest. They practically disappeared under treatment.

DR. HARRY E. ALDERSON: I have seen many patients with lesions of this character but not in such great number. It is interesting to speculate whether the primary lesion is congenital or whether there is, in addition, an occupational influence, or whether the habits of the patient, the personal hygiene, may be factors. The treatment is simple, consisting in emptying the cysts, cauterizing the larger ones and teaching the patient how to keep himself clean. The patient is a university graduate and an iceman. I wonder whether his occupation has anything to do with his condition.

MORPHEA. Presented by DR. HARRY E. ALDERSON.

An American electrician, married, aged 50, presents a typical linear lesion of morphea extending from the left posterior parietal to the left frontal region. The patch is about 6 cm. in length and 1 cm. in width. It has been present for nine years. The patient is bald. Prior to an accident there was nothing wrong with his scalp. He struck his head violently against a beam. The skin was not broken, but marked ecchymosis developed and persisted in the area for several months. Then the elongated typical morpheic lesion slowly developed. It is smaller now, being about half its original size. There are no disturbances in sensation.

The patient's past history and physical condition reveal no evidence of endocrine dysfunction, and nothing has been observed that would indicate the presence of an underlying predisposing pathologic condition.

DISCUSSION

DR. HARRY E. ALDERSON: This case is interesting in view of the published reports of scleroderma caused by damage to the nerves. In this case the lesion appeared at the actual site of injury. Treatment has consisted in the use of nonirritating oils.

KERATOSIS FOLLICULARIS. Presented by DR. N. N. EPSTEIN.

E. V., a married white woman, aged 21, states that about three or four years ago she first noticed what appeared to be a few freckles over the forehead, which gradually spread down the neck. Lesions appeared on the chest one year ago. The small dark spots became papular and scaly, with a small depression in the center. The condition disappeared spontaneously on two occasions.

The urine and the blood were essentially normal. The Wassermann reaction was negative. The patient has a coincidental congenital cardiac lesion. On microscopic examination my associates and I thought that the lesion was one of keratosis follicularis.

DISCUSSION

DR. HARRY E. ALDERSON: On looking the patient over more carefully, one sees that the lesions are small, and in this light some appear to be telangiectatic. At first the papules looked like follicular seborrheids, but the entire condition may have been modified by pregnancy. The biopsy specimen taken several months ago showed a picture like that of keratosis follicularis. I favor that diagnosis.

DR. H. E. MILLER: The absence of itching and the presence of seborrheid-like patches in the scalp tend to confirm the diagnosis of keratosis follicularis. The results of biopsy were characteristic of that disease.

MINNESOTA DERMATOLOGICAL SOCIETY

LOUIE H. WINER, M.D., *Secretary*

Meetings of Sept. 13 and Oct. 4, 1933

D. D. TURNACLIFF, M.D., *President*

LOCALIZED MYXEDEMA. Presented by DR. S. E. SWEITZER, Minneapolis.

The patient, a fairly well developed man, aged 62, presents lesions on the lower parts of the legs. He says that he had a subtotal thyroidectomy in 1917 and a second operation in 1926 because of a return of the goiter. About 1931, he says, the legs began to swell, following which numerous lumps appeared below the knees. Over the tibial crests are numerous reddish nodules, varying in size from that of a pea to that of a nut, and moderately firm. On palpation the lesions give the impression of being filled with fluid. There is a plaque about 3 by 3 cm. on the right great toe and there are others on the calf of each leg. The rest of the body is free from infection. The basal metabolic rate was found to be plus 65. There are slight exophthalmos and slight tremor of the hands. A biopsy specimen is shown.

DISCUSSION

DR. L. A. BRUNSTING, Rochester: The lesions on the legs are unusual in extent and in resemblance to lymphangioma circumscriptum. On the posterior aspects of the calves are brawny, indurated plaques such as those which characterized the cases described by O'Leary.

DR. HAMILTON MONTGOMERY, Rochester: In none of the cases reported by Dr. O'Leary in his paper, "Localized Solid Edema of the Extremities in Association with Exophthalmic Goiter," was the basal metabolic rate so high as in this case. Perhaps the rate of plus 65 per cent in the patient presented here accounts for the fact that the cutaneous lesions are more marked, even to the extent of simulating lymphangioma circumscriptum. The histopathologic sections are typical, however, of so-called localized myxedema. I believe that there will be no difficulty in demonstrating mucin in the sections if a stronger mucicarmine stain is used.

DR. S. E. SWEITZER, Minneapolis: This patient came into the office, and I asked Dr. Butler, Dr. Winer and Dr. Lynch to see him. Dr. Butler suggested that the patient might have a goiter with slight exophthalmos. The diagnosis was then easy. Biopsy was performed, and mucin was present. This disorder is rare. In an article by Ingram in the *British Journal of Dermatology* twenty-six cases are listed. This case is the twenty-seventh.

A CASE FOR DIAGNOSIS. ANGIOLUPOID OF TERTIARY SYPHILIS (?). Presented by DR. H. E. MICHELSON, Minneapolis.

In this woman, aged 38, pulmonary tuberculosis with cavitation was diagnosed at the state sanatorium. The Wassermann reaction was negative. The lesion consists of a firm induration of the alae of the nose and of the terminal portion of the septum, producing an enlargement of the entire nose. There are no lupoid nodules, but there is some scarring on the right side, without visible ulceration. The consistency is firm. Two injections of bismuth and one of neoarsphenamine have as yet produced little effect on the lesion, but treatment was instituted only five days before presentation. Microscopic sections showed a chronic type of inflammation with epithelioid and giant cells but no tuberculoid formation. The diagnosis microscopically was indeterminate.

In spite of the diagnosis of tuberculosis and the negative Wassermann reaction, the lesion seems to me to be a chronic syphiloma because of the induration of all of the tissues, the scar formation and the lack of definite tuberculous tissue. I think that the response to treatment will be a deciding factor in arriving at a final diagnosis.

DISCUSSION

DR. HAMILTON MONTGOMERY, Rochester: I agree with Dr. Michelson. In this infiltrated type of tertiary syphilis the therapeutic response may be slow. The histologic sections do not suggest tuberculosis, nor are they typical of a syphilitic process.

DR. J. F. MADDEN, St. Paul: Chronic inflammation and stasis secondary to chronic sinusitis and rhinitis can produce a cellulitis similar to that in this picture. This is a possibility that should not be overlooked.

DR. L. A. BRUNSTING, Rochester: It is my impression that part of the picture is due to stasis with lymphedema, such as occurs frequently when there is chronic granulation involving the legs or genitalia, with obstruction to the return flow of lymph. Otherwise there is no particular choice between syphilis and tuberculosis.

LYMPHOGRANULOMA INGUINALE. Presented by DR. S. E. SWEITZER, Minneapolis.

The patient, aged 26, states that he had herpes of the penis and phimosis, following which there was a bilateral enlargement of the inguinal lymph nodes. The enlargement increased, and the nodes on the right side suppurated and were incised. The dark-field examination and the Wassermann test gave negative results. The bacillus of Ducrey was not found. Frei tests with material supplied by the University Hospital were strongly positive. With material obtained from the suppurating gland more Frei antigen was prepared following the technic described by Frei. This material gave positive cutaneous reactions in the patient and negative reactions in ten controls. Two doses of one-fourth skin unit of roentgen rays were given over the involved glands, with decrease in the inflammatory reaction.

Physical examination at that time revealed a well nourished young man who was up and about the ward. The only lesion that could be seen was the incision over the right inguinal lesion, with induration of the edges. The increased pigmentation of the skin was due to the topical application of a 1 : 5,000 solution of potassium permanganate.

I think that this is the first case of lymphogranuloma inguinale to be recognized in Minnesota. The period of incubation is short. The patient gave a positive reaction to the Frei test. He has improved considerably under treatment with an antigen and roentgen rays.

MYCOSIS FUNGOIDES. Presented by DR. S. E. SWEITZER, Minneapolis.

W. C., aged 69, was first seen in May, 1933, at which time he complained of several painful ulcerated cutaneous nodules on the anterior surface of the left thigh. At that time the Wassermann and Kahn tests and roentgenograms of the chest gave negative results, and biopsy was not diagnostic. Two Mantoux tests were strongly positive. The patient received one-half skin unit of roentgen rays and left the hospital against advice. On his return to the hospital in August, 1933, he stated that following his previous hospitalization the lesions diminished in size for a time, but that after about two weeks they again began to increase. Physical examination at the time of reentry to the hospital revealed a white man who was up and about. There were no findings except the lesions on the anterior surface of the left thigh. Here there were three pedunculated lesions, which were about 2.5 cm. in diameter and about 2 cm. in height. Each had a necrotic center and discharged a thick, greenish, serous-like material. The fourth lesion was just appearing; it rapidly developed into a miniature of the larger lesions. The left inguinal lymph nodes were slightly enlarged. The primary lesions were localized to the skin and were freely movable and only slightly painful. The larger of the lesions, as well as one of the left inguinal nodes, was removed for microscopic study.

DISCUSSION

DR. HAMILTON MONTGOMERY, Rochester: Clinically, this case presents the features of mycosis fungoides d'emblée. Histologically, the sections show all of the features of lymphoblastoma. It is necessary to make a detailed morphologic study under high power or with an oil immersion lens in order to distinguish between the clumping of cells seen in mycosis fungoides and the Dorothy Reed cells of Hodgkin's disease.

DR. L. H. WINER, Minneapolis: It is interesting to note the various opinions given by pathologists on the section. Dr. Bell thought that the condition was Hodgkin's disease, but when I asked him about mycosis fungoides he said that he did not know its pathology. Dr. Lufkin, of the Minneapolis General Hospital, said that he thought that the condition was not Hodgkin's disease but some form of chronic granulation. I looked at the slide and saw all the eosinophils. Today Dr. Michelson pointed out what looked like a large monocyte; Kyrle has said that if one finds a large monocyte the differential diagnosis is made. We treated the patient with roentgen rays. We gave him 1 skin unit of roentgen rays about three months ago and were going to give him more, but, dissatisfied, he left the hospital. I am of the opinion that the condition is mycosis fungoides.

DR. HAMILTON MONTGOMERY, Rochester: I have studied more than one hundred and fifty cases of lymphoblastoma of the skin. I do not believe that the large monocyte can be used in distinguishing between mycosis fungoides and Hodgkin's disease, as it is present in both. The clumping of cells seen in mycosis fungoides is composed of endothelial-like cells with pale-staining nuclei and nucleoli, in contrast to the irregular, densely staining, large nucleolus in the Sternberg or Dorothy Reed cell of Hodgkin's disease.

NOTE.—After further detailed study of the sections in this case, I believe that the histopathologic picture is that of mycosis fungoides in the tumor stage, and that it shows an early lymphosarcomatous change.

ACUTE ALCOHOLIC PELLAGRA. Presented by DR. S. E. SWEITZER, Minneapolis.

The patient, aged 54, states that he was on an alcoholic debauch for several days before admission to the hospital. He took no food during the five day period and while sleeping during the day exposed himself to the sun. The stimulant used was denatured alcohol. There was a history of chronic alcoholism.

On admission to the hospital he was visibly nervous and weak. His eyes were unsteady and the conjunctivae congested. His tongue was red and tender. The gastro-intestinal tract was moderately upset. There was no evidence of dementia. The cutaneous lesions consisted of two enormous bullae filled with clear serum on the dorsa of the hands.

A diet high in vitamins and ointment of boric acid, U. S. P., applied to the hands have resulted in the picture which the patient now presents, after twelve days of hospitalization.

DISCUSSION

DR. L. A. BRUNSTING, Rochester: I think that the condition in cases of this sort is pellagra and not pseudopellagra. In patients in this condition there is an unusually high percentage of achlorhydria.

DR. S. E. SWEITZER, Minneapolis: Boggs and Paget gave an analysis of cases of pellagra encountered at Johns Hopkins Hospital during twenty years, and they arrived at the conclusion that alcoholic pellagra is true pellagra. At present I think that some patients may show some of the symptoms of pellagra more markedly than others; some patients have lesions of the tongue and diarrhea, while others have not; some have mental stupor, while others have not.

DR. L. A. BRUNSTING, Rochester: The diagnosis of this condition is usually missed because pellagra is not thought of, particularly in regions where the disease is not endemic. Since 1920 we have seen one hundred and thirty-five cases of pellagra at the Mayo Clinic; most of the cases were of the secondary type and occurred in patients who came chiefly from the states of the Middle West and the Northwest and Canada.

DR. S. E. SWEITZER, Minneapolis: We had fifty-eight cases up to last spring and six more cases this summer.

PEMPHIGUS VULGARIS. Presented by DR. J. F. MADDEN, St. Paul.

H. P., a storekeeper, aged 70, noticed an eruption on the arms and trunk during June, 1933. It appeared as asymptomatic blisters of various sizes. The lesions became more numerous until most of the cutaneous surface was involved. In July, the patient began to complain of weakness and loss of weight. The symptoms progressed until August, when he was admitted to Ancker Hospital. He had lost 20 pounds (9 Kg.) and was unable to retain food; he was so weak that he could not walk. The eruption was generalized, but there were few lesions on the mucous membranes. The lesions varied from vesicles the size of a pea to bullae the size of an egg. The skin had been denuded at the sites of old lesions, and a raw, weeping surface remained. Nikolsky's sign was present.

The patient was treated with 15 drops of viosterol three times a day and given a diet high in fats and carbohydrates. He improved rapidly. The eruption had entirely involuted and he had gained 10 pounds (4.5 Kg.) by September 15. Treatment was continued. A new crop of lesions began to appear on about October 1.

The blood showed an eosinophil count of from 12 to 15 per cent. The hemoglobin was 67 per cent on admission and is now 82. The red blood cells numbered 3,500,000 on admission and now number 4,500,000. The urine showed a trace of albumin. The Wassermann test of the blood was negative.

DISCUSSION

DR. F. R. WRIGHT, Minneapolis: The patient has a vesicle typical of pemphigus on the inside of one ankle.

DR. J. F. MADDEN, St. Paul: The patient was delirious and too weak to walk on admission to the hospital. The eruption involved almost the entire cutaneous surface. Viosterol was given in doses of 15 drops three times a day, and the patient was given a diet high in carbohydrates and fats. The eruption has been involuting, and the patient has been gaining strength and weight. New lesions began to appear about four days ago.

KRAUROSIS VULVAE. Presented by DR. J. F. MADDEN, St. Paul.

Mrs. M. W., a housewife, aged 44, states that she first noticed severe itching about the external genitalia two years ago. The pruritus was so marked that it interfered with her sleep and was a constant annoyance during the day. The itching increased in severity at times. The pruritus was followed by swelling of the external genitalia and chronic dermatitis. The eruption now involves the genitalia and crural region. The labia are atrophic. There are white, pea-sized atrophic spots on the labia majora and crural region. There are larger leukoplakic plaques on both labia associated with excoriations and chronic dermatitis. A biopsy specimen is shown.

DISCUSSION

DR. H. E. MICHELSON, Minneapolis: When the members discuss the white spot diseases the conditions in the cases in question are usually the end-results of the processes. Therefore, clinically, it is difficult to make a positive diagnosis. In lichen sclerosis there are usually lesions near the clavicle. There may or may not be plugging, the absence of which is more important than its presence. What the microscopic section may reveal depends, to be sure, on the stage of the disease when the biopsy was made. To me, the typical sclerotic type of lichen can be identified when the section shows a homogeneous band between the atrophic epidermis and the well marked, sharply demarcated, narrow zone of infiltrate corresponding to the lower plane of a lichen planus infiltrate. In the case presented I think that the intense itching and the lesions at the wrist favor the diagnosis of lichen planus with atrophy. One must recall that the lesions of lichen planus and lichen sclerosis have been noted in the same patient.

DR. S. E. SWEITZER, Minneapolis: I thought that the patient had lichen albus because of the lack of color. If itching is present, there is a possibility that the condition is lichen planus or in the same group.

DR. HAMILTON MONTGOMERY, Rochester: I have recently been studying the clinical and histologic differentiation between kraurosis vulvae, leukoplakia and pruritus vulvae, as well as their differentiation from various dermatoses. Clinically, I believe that this case is one of lichen sclerosis atrophicus, and I thought that I saw definite plugs in a few of the lesions. The histopathologic picture as shown in the sections would be satisfactory for either kraurosis or lichen sclerosis or atrophicus, which may be indistinguishable histologically from each other. The histologic picture is characterized by edema with transudation of serum just beneath the epidermis, resulting in flattening of the rete ridges, liquefaction necrosis of the basal cell layer and atrophy of the prickle cell layer. Beneath the transudate homogenization of the connective tissue is seen. The elastic tissue is separated from the epidermis by the edema, but is not destroyed. Both lichen sclerosis et atrophicus and kraurosis may present a considerable amount of infiltrate in the deeper portions of the cutis or at the margins of the process, but in certain stages little infiltrate may be seen. The histopathologic picture seen in this case is not that, I believe, of an atrophic lichen planus. Lichen sclerosis involving the vulva has been described previously (ARCH. DERMAT. & SYPH. **5**:786 [June] 1922). I recognize that the distribution of the lesions on the arms and in other places suggests more the atrophic type of lichen planus, but I feel that the clinical appearance of the individual lesions together with the histopathologic picture of tissue from the labia strongly supports the diagnosis of lichen sclerosis atrophicus.

HERPES GESTATIONIS. Presented by DR. J. F. MADDEN, St. Paul.

Mrs. J. J., a housewife, aged 25, states that the eruption first appeared during the fifth month of her first pregnancy. The lesions increased in number until the seventh month. The eruption remained about the same, with new lesions appearing and others involuting, until ten days after parturition. Then involution began and was complete about two months post partum. The patient experienced no marked discomfort except from ruptured bullae on points of pressure and in the flexures. The mucous membranes were free. The eruption was generalized, but most marked on the trunk. The lesions were vesicles and bullae varying in size from that of a pea to that of a silver dollar, and were in all stages of evolution and involution. They were symmetrical and grouped, and not painful. The fluid in the bullae was at first clear, then milky and finally purulent. Some of the bullae ruptured and left a raw, denuded surface.

The pregnancy was uneventful and took the usual course. The baby was normal.

DISCUSSION

DR. S. E. SWEITZER, Minneapolis: I remember that one of my patients during pregnancy had a marked vesicular eruption on the arms, and eruptions like it had occurred in her previous pregnancies. The condition resembled dermatitis herpetiformis but was not that disease. When the child was delivered the condition cleared up.

HYDROA AESTIVALE. Presented by DR. H. E. MICHELSON, Minneapolis.

The patient, aged 20, states that his eruption began eight years ago with vesiculation on the arms and face following an exposure to sunlight and a subsequent sunburn. There has been no period in which he has been free from the eruption since its inception, but it has been more noticeable in the early part of each summer. The lesions are limited to the face, neck, ears and extensor surfaces of the arms. They consist of pea-sized, dark-colored papules, vesicles and white scars. No hematoporphyrin was found in the urine. The patient reacted strongly to ultraviolet radiation on the back, and biopsy showed an intense reaction of the epidermis with formation of vesicles and a tendency toward necrosis.

DISCUSSION

DR. F. W. LYNCH, St. Paul: Dr. O'Leary mentioned the basic resemblance of this condition to xeroderma pigmentosum. There are, however, important differences. There is probably a difference in the underlying hereditary tendency in that hydroa shows a predominance in males which is not found in xeroderma. The constant absence of porphyrinuria in xeroderma is also an essential difference. In both diseases there is sensitivity to solar radiation, but the eruption of hydroa is evoked by the ultraviolet rays of longer wavelength, which are unable to produce lesions in patients with xeroderma. My associates and I gave heavy doses of ultraviolet radiation in a case of xeroderma and were unable to produce bullae, while such lesions are characteristic of hydroa and have been present in this patient in the past.

DR. H. E. MICHELSON, Minneapolis: I believe that this case belongs to the hydroa aestivale group, and I must emphasize that hematoporphyrin may be found in the urine of a patient with this disease in the early years of life and may disappear from the urine as the patient gets older, while the condition of the skin continues to show lesions of hydroa aestivale. Dr. Lynch, of my department, has completed some work on sensitization to the various wavelengths of the spectrum, especially in xeroderma pigmentosum, and has cited the findings in hydroa aestivale also. The paper will be published in the near future.

PHILADELPHIA DERMATOLOGICAL SOCIETY

R. L. GILMAN, M.D., *Secretary*

Sept. 29, 1933

J. P. GUEQUIERRE, M.D., *President*

INTERSTITIAL KERATITIS WITH SCARS OF TERTIARY SYPHILIS. Presented by DR. J. V. KLAUDER.

A man, aged 25, presents polycyclic, pigmented, atrophic scars of annular configuration on the upper third of the right leg. The appearance suggests the remains of tertiary syphilis. The ulcers began insidiously five years prior to presentation, and lasted for four or five months. The patient had active interstitial keratitis of both eyes. The Wassermann and the luetin tests were positive. Among 250 patients with interstitial keratitis studied at Wills Hospital, this patient is the only one in whom there is evidence of cutaneous involvement with syphilis.

PELLAGRA SECONDARY TO ALCOHOLISM. Presented by DR. V. C. GARNER.

A man, aged 29, presents sharply marginated, erythematosquamous patches of dermatitis of various sizes, involving the neck, shoulders, back, forearms and hands. The large circular lesion on the back is approximately 12 inches (30.48 cm.) in diameter. All the lesions show a distinct erythematous flare at the borders and abundant scale with a tendency toward central fading. The dorsa of the hands, wrists and forearms are involved in an erythematosquamous gauntlet sharply marginated above the elbows. The lower extremities and face are entirely clear. There are objective as well as subjective evidence of mild glossitis and a history of diarrhea. The condition began two weeks before presentation, following an alcoholic debauch of three weeks' duration, with very little food during that time. There is evidence of slight peripheral neuritis. The pupils are unequal.

The Wassermann reaction is negative. The blood count shows moderate secondary anemia. No fungi can be demonstrated.

DISCUSSION

DR. J. V. KLAUDER: I cannot be certain of the diagnosis of pellagra from the cutaneous picture. The eruption on the back is unusual for pellagra. There is unusual involvement of the unexposed parts of the body with little involvement of the exposed parts.

DR. A. STRAUSS: I think that the hands present a good picture of the alcoholic type of pellagra. Of course, the lesions on the body are rather unusual, but in certain lights they have that peculiar mahogany color which is presented by pellagra. I do not know why the man couldn't have been exposed to the sun in those parts as well as in the more usual areas because I don't believe that he knew what he was doing if he drank as much alcohol as he said he did.

DR. V. C. GARNER: I wish that Dr. Klauder would suggest an alternative diagnosis.

DR. J. V. KLAUDER: A diagnosis of pellagra is to be considered; it is reasonable, since the condition appeared after an alcoholic debauch. I don't think, however, that that necessarily warrants the diagnosis. It could be a sharply marginated eczema.

DR. H. J. SMITH: This summer we have seen some peculiar eruptions from alcoholic debauches. Perhaps the kind of alcohol had something to do with the disorder. The eruption on the hands and wrists looked like pellagra; that on the trunk did not.

DR. E. F. CORSON: The patient said that he had been exposed to strong sunlight with only a thin undershirt as protection. One might get some effect through a thin garment. Women are occasionally sunburned through a thin waist.

DR. PATRICIA DRANT: I thought that he had been in a rather hazy mental condition for a period of time.

DR. V. C. GARNER: The idea of the instrumentality of sunlight in the production of pellagra must be revised. Cases are seen at times in which the eruption is typical over the feet and ankles on men who never go barefoot, and some of the textbooks picture lesions on the trunk and back. In this case it seemed the most logical diagnosis.

SENEAR-USHER SYNDROME. Presented by DR. E. F. CORSON.

A night watchman, aged 60, presents an eruption of ten months' duration. It started in the left inguinal region, where he had a hernia and pressure from a truss, spread to the face, where a butterfly configuration is evident at times, then to the neck, shoulders and elsewhere. The contents of the bullae are sterile. No biopsy has been made. His teeth are very bad, with marked periodontitis.

DISCUSSION

DR. J. V. KLAUDER: That same patient was under observation at the Philadelphia General Hospital. I think it is a typical instance of the Senear-Usher syndrome.

JUXTA-ARTICULAR NODULES OF LUTZ-JEANSELME. Presented by DR. COBANE for DR. S. S. GREENBAUM.

A man, aged 34, a laborer in a coal yard, presents subcutaneous, solitary nodules the size of a walnut on the extensor surfaces of both forearms and on the left hip, of eight years' duration. The nodules are not attached to the skin. They are painless, not tender and nonfluctuating. The nodule on the left forearm was removed surgically for study of the pathologic process. The microscopic examination revealed a fibroma, considerably vascular, showing perivascular infiltration by small lymphocytes and plasma cells.

The Wassermann reaction of the blood in July, 1933, was positive. The spinal fluid in August, 1933, was normal. The treatment consists of 100 mg. of bismocymol, administered intramuscularly once a week, of which the patient has had eight injections since his admission to the hospital in July, 1933.

DISCUSSION

DR. J. H. COBANE: The case is interesting because it is the third instance of the juxta-articular nodules of Lutz-Jeanselme that we have seen in the past eighteen months. About ninety-two cases have been recorded in the literature since the condition was first described in 1899. At that time there was trouble in determining the etiology. At first the nodules were thought to be due to bites of insects, but since the Wassermann reaction came into use, making the diagnosis of syphilis more exact, the last thirty cases described in the literature have all been recorded as occurring in persons with syphilis. Trauma seems to play an important part. In this instance the lesions are the only sign of syphilis, outside of a positive Wassermann reaction, that was found. The patient had eight injections of bismocymol, 100 mg. per week, and the nodules have involuted, the one on the right arm at least 50 per cent, while the one on the hip has disappeared entirely.

NEUROTIC EXCORIATIONS. Presented by DR. J. V. KLAUDER.

A man, aged 62, presents scattered excoriations of the punch variety, not scratched, involving chiefly the legs, of three years' duration. The areas are extremely pruritic. The patient states that he woke at night to find himself "digging." He has an anesthetic sclera and pharynx.

DISCUSSION

DR. J. V. KLAUDER: The most interesting point about this patient is that he has an anesthetic conjunctiva and hard palate. I find that condition present in most patients with neurotic excoriations and in a certain type of patient with pruritus. It is a very important finding in the examination of these patients.

DR. A. STRAUSS: The case impressed me from the history as one of dermatitis herpetiformis. There are a great many lesions on the lower part of the arm and a number of depigmented areas, with a number of darkly pigmented areas around these depigmented areas. The duration of the disease, the whole picture, impressed me as that of one of the milder types of dermatitis herpetiformis rather than of neurotic excoriations.

DR. D. M. PILLSBURY: I should like to suggest the remote possibility of this being an adult type of lichen urticatus. The distribution is suggestive, the process being limited to the extremities and the upper part of the back. The patient states that the condition is somewhat worse in warm weather. This diagnosis is possibly rather far-fetched, but is to be considered.

DR. J. V. KLAUDER: I do not believe that the eruption is that of Duhring's disease for the following reasons. There is an absence of vesicles, and a history of their absence. The distribution is not that of Duhring's disease, and there is no grouping of the lesions. The eruption is not as symmetrical as that of Duhring's disease. The lesions are sharply marginated, "punched out" excoriations, which are not characteristic of Duhring's disease.

FOX-FORDYCE DISEASE. Presented by DR. D. M. PILLSBURY.

A colored man, 35 years old, presents a highly pruritic folliculopapular eruption, limited to the axillae, nipples and suprapubic region. There was considerable hyperpigmentation in the affected areas when the patient was first seen. The Wassermann reaction of the blood is negative, as is also that of the spinal fluid.

The eruption is of approximately eighteen months' duration and has responded markedly to a total of 2¾ skin unit dose of unfiltered roentgen rays. The patient gave a history of having received antisyphilitic therapy in 1926; on the basis of this finding he has received a total of forty-five injections of neoarsphenamine and forty-seven injections of bismuth salicylate. He has always been seronegative while under my observation.

A CASE FOR DIAGNOSIS: LICHEN PLANUS HYPERTROPHICUS. Presented by DR. R. L. GILMAN.

A woman, aged 70, presents a weltlike pruriginous eruption of the dorsum of the right forearm of five years' duration. She has also a slight excoriated papular eruption in the occiput. There is possibly a factitial neurotic element present.

DISCUSSION

DR. V. C. GARNER: I thought that it was lichen planus hypertrophicus.

DR. E. F. CORSON: I came to the same conclusion, although it is certainly a bizarre case. Usually in such instances one finds hypertrophic lesions on the lower part of the legs. There is nothing in the mouth and there are no young, shiny papules on the skin, but there are a purplish color and linear lesions which suggest the diagnosis.

ABORTIVE RECKLINGHAUSEN'S DISEASE AND GRANULOMA INGUINALE. Presented by DR. S. S. GREENBAUM.

A woman, aged 30, presents several small, soft, sessile tumors, some pedunculated, on the trunk and extremities, present since birth. Some of the tumors show herniation. They are painless and not tender. Some of them are thought by the patient

to be enlarging. The patient also presents a patch of small, discrete, brown pigmentary spots over the left side of the chest (infra-axillary area). She gives a history of having had three children who are living and well and two miscarriages. The familial history is unimportant. Six years before presentation the patient had a vulval lesion, and four years previous to presentation she had two intramuscular and forty-eight intravenous injections. The pupils are equal and regular and react well to light. The tendon reflexes on the left side are stronger than those on the right side. The Romberg sign is normal. The Wassermann reaction of the blood is negative. The blood cholesterol is 480 mg. per hundred cubic centimeters. The patient also shows an irregular, superficially eroded, red granuloma extending peripherally in the left labial inguinal area. There is a vaginal discharge produced by endocervicitis.

DISCUSSION

DR. A. STRAUSS: Why is the term "abortive" used? There are some typical lesions and pigmented areas which suggest that the disease may go further.

DR. J. H. COBANE: The word "abortive" was used because of the small size of the lesions and their scarcity.

DR. D. M. PILLSBURY: I was struck with the resemblance of the nodular lesions to Schweninger-Buzzi's disease. I think certainly that the lesions which are present, namely, the nodules and pigmentation, are entirely typical of fully developed Recklinghausen's disease, although the eruption itself is sparse.

DR. V. C. GARNER: I agree with Dr. Strauss that we shouldn't call this abortive Recklinghausen's disease. Eller, in his paper, used the term "atypical," or "*forme fruste*," for cases that present simply pigmented spots, usually appearing in families in which some of the relatives have typical Recklinghausen's disease.

A CASE FOR DIAGNOSIS. Presented by DR. A. STRAUSS.

A white girl of 18 has a swelling of both hands of six months' duration. Roentgen examination shows no abnormality. The Wassermann reaction of the blood was negative.

DISCUSSION

DR. V. C. GARNER: I suggest tuberculous tenosynovitis.

DR. J. V. KLAUDER: Lupus pernio is to be considered. Her circulation is like that in chilblains. She has the cyanotic fingers that make this diagnosis somewhat reasonable. Herr hands are purplish red and cold to the touch.

DR. J. P. GUEQUIERRE: She states that she has had cold hands and feet since some time prior to her injury. That would fit in with a diagnosis of lupus pernio.

DR. A. STRAUSS: This patient has been thoroughly examined from every point of view. There is no evidence of tuberculosis in any other part of the body. There have been two negative Wassermann tests. The tuberculin test and the roentgenogram of the chest show no evidence of tuberculosis. There is a suggestive but not typical Hutchinson tooth; that is why we have done the large number of Wassermann tests.

DR. E. F. CORSON: The suggestion of Dr. Garner is worth while. Roentgen examination did not show any evidence of a pathologic process in the bones, which one would take to be present on superficial examination. There is thickening that might include the periosteum. The roentgenogram was looked over by surgeons who saw nothing requiring surgical intervention.

A CASE OF THE REMOVAL OF GUNPOWDER BY TREPHINING. Presented by DR. S. S. GREENBAUM.

A girl, aged 6, was burned on the left cheek and neck by an exploding blank shot from a 32 caliber revolver, accidentally discharged by her brother. Attempts at curettage and scrubbing have been unsuccessful.

DISCUSSION

DR. J. V. KLAUDER: It wasn't quite clear to me what result was shown. All I saw was powder marks on the side of the face.

DR. J. H. COBANE: This patient was admitted to the clinic for surgical conditions. There they scrubbed the area and tried to remove some of the powder by curettage, to no avail. She was sent to the clinic for diseases of the skin for suggestions. Dr. Greenbaum had some 0.5 mm. cutaneous trephines manufactured and used them in the ordinary dental engine. He had to use a general anesthetic for the youngster, but I think that the work could be done under local anesthesia in an adult. Each little spot was trephined slightly and then picked up with forceps and snipped off with ophthalmic scissors. About eighty of the larger spots were removed. We tried this on the neck in the thought that if there were scarring it would not make so much difference. Since eighty were removed in about fifteen minutes, we thought that maybe the entire number could be removed in four or five more sittings. The trial succeeded very well. There are only pink scars remaining, and these are level with the normal skin.

DR. D. M. PILLSBURY: I presume that the apparatus was that designed by Urbach for taking biopsy specimens for chemical analysis.

DR. J. P. GUEQUIERRE: Urbach's instrument came to my mind when Dr. Cobane spoke. He used it for biopsy specimens and also in treating furunculosis.

DR. E. F. CORSON: When looking up another subject I ran across an article by E. L. Keyes the elder in which he described a procedure the same as this though carried out with a hand-operated cutaneous punch. It was in the *Journal of Cutaneous and Genito-Urinary Diseases,* March, 1887. Keyes had used the punches since 1879, and related that a German, Busch, in 1884 advised that such a punch be attached to a dentist's drill engine. Keyes reported good cosmetic results from this procedure. Dr. Greenbaum is to be commended on reviving a satisfactory form of therapy.

NEW YORK ACADEMY OF MEDICINE, SECTION OF DERMATOLOGY AND SYPHILIS

LEO SPIEGEL, M.D., *Chairman*

Regular Meeting, Oct. 3, 1933

EUGENE TRAUB, M.D., *Secretary*

SARCOID OR LUPUS VULGARIS (?). Presented by DR. FRANK VERO.

P. H., a woman aged 25, born in Turkey of Greek parents, has had an oval-shaped lesion situated near the root of the nose, extending toward the inner canthus of the left eye, for one year. The lesion is 1.5 cm. in its longest diameter. It is yellowish red. It is markedly infiltrated, being raised above the surface, and shows a slight depression in the center. There are a few telangiectases in the lower portion of the lesion. The Wassermann reaction was negative. The results of the roentgen examination of the chest were negative. A tuberculin test was not made.

Biopsy disclosed moderate hyperkeratosis and an epidermis which had undergone atrophy through pressure. The corium showed numerous blood vessels and diffuse infiltration by polymorphonuclears, numerous lymphocytes and plasma cells. Scattered through this infiltrate were small epithelioid tubercles. Some of the deeper vessels showed marked thickening of their walls. In some places the epithelioid cells seemed to be fused, and suggested the formation of giant cells. An occasional giant cell was seen. A follicular funnel showed marked dilatation and

was filled with a plug of keratin. The sections did not represent a sarcoid; the picture was that of lupus vulgaris. The acid-fast stain showed no organisms. A diagnosis of lupus vulgaris was made by Dr. Machacek.

DISCUSSION

DR. ISIDORE ROSEN: I incline to the diagnosis of sarcoid rather than to that of lupus vulgaris. The raised, infiltrated, slightly inflammatory character and the yellowish tinge of the lesion, with the central depression, are suggestive of sarcoid rather than of lupus vulgaris.

DR. LOUIS CHARGIN: I agree with Dr. Rosen. In the face of a histologic diagnosis of lupus vulgaris, one must be cautious in offering another diagnosis. Yet on clinical grounds this seems to be warranted. A revaluation of the histologic observations is indicated.

DR. SAMUEL PECK: A study of tuberculin allergy in this case would be of great interest and perhaps of diagnostic value. Sometimes one sees a mixture of sarcoid-like features in lesions typical clinically of lupus vulgaris. Further histologic study then reveals the typical structure of lupus vulgaris.

DR. SIGMUND POLLITZER: The uniformity in color and consistency speaks in favor of a diagnosis of sarcoid.

DR. FRANK VERO: I saw this patient four weeks ago, and the clinical picture has since changed. The lesion was then sharply defined, elevated and of firm consistency, with a marked depression in the center. Under diascopic examination the lesion appeared to be a diffuse yellowish brown. I favored the diagnosis of sarcoid, yet the histologic observations were characteristic of lupus vulgaris. The lesion has improved somewhat; it is much flatter, possibly owing to the salt-free diet.

PARAPSORIASIS LICHENOIDES CHRONICA WITH SEVERAL VARIOLIFORM LESIONS. Presented by DR. PAUL GROSS.

M. P., a woman aged 25, born in the United States, has had a generalized eruption, except on the face, for several years. It has shown improvement during the summer on the parts of the body exposed to the sun. The patient has not complained of itching.

There are, especially on the flexor surfaces of the forearms, small glistening lichenoid papules almost the color of the skin, also guttate lesions the size of a lentil, which are scaling or which yield scales when scraped with the finger-nail. These are brownish red. On the flexor surface of the left forearm are two purplish papules with darker centers, resembling the lesions of the varioliform parapsoriasis.

DISCUSSION

DR. SIGMUND POLLITZER: This patient has an extensive distribution of lesions on the trunk, particularly on the lower part of the torso, resembling a few lesions on the arm. I agree with the diagnosis. The absence of subjective symptoms and the appearance of the lesions are sufficiently characteristic.

DR. ADOLPH ROSTENBERG: Does the severe itching speak against the diagnosis? Recently I had a case which clinically fitted in with this group, but there was severe itching.

DR. SIGMUND POLLITZER: Yes, severe itching would be contrary to the diagnosis. An unusual feature is that on the girl's thighs, which are well tanned by exposure to the summer sun, there are a number of whitish spots which are in general the size of the lesions which she has elsewhere. She says that these spots represent areas where she formerly had lesions.

DR. PAUL GROSS: The lesions have disappeared where the skin was exposed to the sun. Whether the depigmentation could be considered as leukoderma is

hard to decide on account of the recent tanning of the skin. But leukoderma is not infrequently observed in both the chronic and the acute type of parapsoriasis lichenoides.

A Case for Diagnosis: Pityriasis Rosea (Papulovesicular Type)? Pityriasis Lichenoides et Varioliformis Acuta? Presented by Dr. Laird S. Van Dyck.

This boy, aged 12, has had an eruption for four weeks. He first noticed some reddish spots on his chest, which spread rapidly over the entire body. There were no subjective symptoms until recently, when there has been slight itching.

There is now a maculopapular and papulovesicular eruption extending over almost the entire body, including the palms and soles. Many lesions on the face and on the back of the scalp are scaly macules. Most of the lesions on the trunk and extremities are discrete reddish-brown papules and papulovesicles. Some are covered with scales and others with crusts. There are areas of depigmentation on the arms and hemorrhagic lesions on the ankles. The Wassermann, Kahn and Kline tests have been negative. The report of the biopsy has not been received.

DISCUSSION

Dr. E. William Abramowitz: I favor the diagnosis of parapsoriasis varioliformis. There are numerous areas of leukoderma, some papulovesicular lesions with crusts, and characteristic pits in some of the lesions that have undergone involution.

Dr. Max Scheer: I agree with the diagnosis of pityriasis lichenoides. There are some dusky red lesions on the flexor surfaces of the forearms which closely resemble syphilitic papules. Such lesions are common in pityriasis lichenoides.

Dr. Isidore Rosen: I agree. In pityriasis lichenoides et varioliformis the eruption rapidly changes in a few weeks and often tends to resolve with the mildest of therapy.

Dr. Paul Gross: When the first case of parapsoriasis varioliformis was presented, the question was raised whether the acute variety belonged in the parapsoriasis group. Since then a number of cases have been presented under that name, and I wonder whether the condition is now accepted as an acute variety of pityriasis lichenoides Juliusberg.

Dr. Walter James Highman: I do not exclude this condition from the parapsoriasis group because the inflammation happens to be exudative. Exudation is present in countless inflammations. The objection lies in the fact that the course of this disease is different from that of the various forms of parapsoriasis. This is far more significant than the accident of the presence of exudation.

Dr. Louis Chargin: I believe that dermatologists will have to modify their view with respect to the curability and the course taken by certain types of parapsoriasis. I refer especially to the guttate, psoriasiform lichenoid and varioliform varieties of the disease. If one examines the literature of the past several years one finds records of cases in which cures occurred either spontaneously or as a result of therapy (administration of pilocarpine hydrochloride or some form of physical therapy). Moreover, the course taken by this disease differs in many instances from that described by teachers many years ago, namely, that of extreme chronicity. In some cases it runs an acute and in some a subacute course, even though in the majority it runs a course that is chronic. Then, too, the condition sometimes recurs. These statements do not apply to parapsoriasis in patches, which remains incurable in nearly all cases, regardless of therapy.

Dr. Walter James Highman: I have read the reports mentioned by Dr. Chargin. Has any one here seen ordinary parapsoriasis cured?

Dr. Laird S. Van Dyck: The eruption on this boy resembles very closely the pityriasis rosea with papulovesicular lesions described by Karl Ullman (*Dermat.*

Wchnschr. **95**:840 [Aug.] 1932). The resemblance is particularly striking in the lesions on the back, palms and soles. This raises the question whether so-called parapsoriasis varioliformis acuta is not simply a variant of pityriasis rosea. The two diseases frequently follow the same course with spontaneous recovery in about two months.

URTICARIA PIGMENTOSA (SOLITARY LESION). Presented by DR. PAUL GROSS.

R. C., a boy 5 months old, was born in the United States. Sixteen days after his birth his mother noticed a lesion on the inner aspect of his left thigh. At times the usually brownish spot resembled a large blister. The lesion is now almost circular, measuring about 2 cm. in diameter, and is light brown with a smooth surface. It is flat, but slightly raised above the surface of the thigh. On friction a red and later white urticarial reaction develops over the entire lesion.

DISCUSSION

DR. LOUIS TULIPAN: I have never seen urticaria pigmentosa manifested in one solitary lesion.

DR. FRED WISE: Dr. Sulzberger called my attention to the absence of pigmentation. Although a diagnosis of urticaria pigmentosa might well be correct, to be determined only by histologic examination, I suspect a more serious possibility, that of amelanotic sarcoma or of sarcoid.

DR. PAUL GROSS: I presented a patient with a similar, small lesion on the wrist four years ago, when this section gave a special clinic for Jadassohn. In that case the diagnosis was proved histologically.

LATE SECONDARY SYPHILODERM RESISTANT TO THERAPY (WITH FINDING OF SPIROCHETES AFTER EXTENSIVE TREATMENT). Presented by DR. A. BENSON CANNON.

This woman, aged 24, colored, was first seen at the Vanderbilt Clinic in May, 1933, at which time she had a 4 plus Wassermann reaction. She received six intravenous injections. Two children (aged 4½ and 3) are apparently well. The patient's present rash started one month ago. In the genital region and on the inner surface of the thighs are numerous large ulcerations and elevated, hypertrophied papules. On the palms are numerous reddish-brown infiltrated papules and pustules. Similar lesions are scattered over the extremities. The reflexes are normal. Blood tests showed the Wassermann reaction to be 4 plus with alcoholic antigen and 4 plus with cholesterol. The Kahn reaction was 6 plus.

Treatment consisted of mercury salicylate and silver arsphenamine. After eight injections of silver arsphenamine (total amount 1.5 Gm.) and six injections of mercury salicylate (7 Gm.) the lesions healed. The patient then interrupted treatment. The blood at that time (August 1) showed a Wassermann reaction of 4 plus with alcoholic antigen and 4 plus with cholesterol and a Kahn reaction of 6 plus.

The patient was seen again on September 20. She reported that one day after the last injection (August 1) a few lesions appeared, which quickly spread over many regions. Lesions ranging in size from that of a pea to that of a dollar could been seen over the right eyebrow, on the right nasolabial region, on the left ear, on both forearms extending to the palms, on the left thigh and on both soles. All showed a markedly infiltrated, sharply outlined circinate periphery and a flat, slightly infiltrated center. A probe test showed 3 plus sensitivity. On the second toe of the right foot and on the fourth toe of the left foot there were deep, painful ulcerations. All the webs showed discoloration and scaling. The condition of one toenail was suggestive of trichophytosis. An examination for tinea gave negative results. The result of dark-field examination of a lesion on the thigh was reported as 1 plus.

On September 27, after one injection of bismuth and a dose of potassium iodide by mouth, the lesions became much flatter and paler. Epithelium formed on the lesion on the thigh. The ulcerations on the webs of the toes healed.

DISCUSSION

DR. ISIDORE ROSEN: Occasionally one sees a patient who fails to respond to the treatment of choice. It is then necessary to change the form of treatment. In this case, I suggest that arsphenamine and bismuth be given instead of silver arsphenamine and mercury. It might also be advisable to stimulate the body to greater resistance by an injection of foreign protein.

DR. LOUIS CHARGIN: I think Dr. Rosen has brought out the important points in connection with the problem. When syphilis becomes recalcitrant to further therapy, it is advisable to change to a remedy that has not been employed in the case. In many instances success is thus attained.

RHINOSCLEROMA. Presented by DR. PAUL GROSS.

E. F., aged 55, Jewish, born in Austria, states that thirty-four years ago a hard tumor was removed from the left side of her nose. For about two years she was free from symptoms. Then the obstruction recurred and some more nodules were removed. Ten or twelve years ago an obstruction developed in the right nostril which has completely closed it. She was treated for two or three years with radium. She had noticed a change in the size and shape of the nose. Two years ago she was again treated with radium and the treatment was continued up to about six months ago. During the first course of treatment with radium (seven years ago) a radium tube was accidentally lost in the nose and had to be found and removed under general anesthesia, which lasted for five hours. A few days later blisters and ulcers appeared on the right side of the nose, which healed within a month but left reddened areas. In the last few months she has noticed the development of "lumps" in this area and has had frequent nosebleed. Pain has been present for two years.

The nose is swollen and deformed, especially in the middle two thirds, but the skin over the area is movable. The tumor mass is of hard consistency. In the right nasolabial region is a purplish-red area where hard nodular lesions can be felt. These are attached to the skin.

The soft palate shows a reddish patch which extends back to the pharynx. The mucous membrane appears sclerosed. The uvula is missing. The soft palate is attached to the posterior wall of the pharynx. There are masses of large nodules on the visible part of the pharynx. The larynx appears to be normal. The ear drums are thickened and retracted.

The Wassermann test was negative. A biopsy was done, and a diagnosis of rhinoscleroma was made. The mucous membrane was composed of a thick, edematous epithelial layer. The stroma was made up of a meshwork of thick connective tissue bundles. In the interstices were masses of plasma cells and numerous large basophilic granules which appeared to be organisms. Colloid bodies of various size were noted. In some places groups of large mononuclear foamy cells were seen.

A second biopsy showed a hyperplasia of stratified squamous epithelium, which was infiltrated by polymorphonuclears and was edematous. The corium was composed of a network of fine fibrils which enclosed numerous nests of foamy cells. Among these cells were structures which were made up of large, round colloid bodies, and others which were composed of numerous small, closely packed, highly refractile, eosinophilic corpuscles. Here and there were foci of infiltration by plasma cells. Elsewhere foci of infiltration by polymorphonuclears were seen. Both plasma cells and polymorphonuclears were also diffusely distributed. The sections were stained by Gram's and Giemsa's methods. Numerous bacilli were seen in the Mikulicz cells in the latter preparations.

DISCUSSION

DR. SIGMUND POLLITZER: Unfortunately I missed this presentation. I do not question that this case is one of rhinoscleroma. I treated a patient with rhinoscleroma about 1907 and thought that the patient was the first with that disease to

be successfully treated with the roentgen rays (*J. Cutan. Dis.* **28**:388 [Aug.] 1910). I discovered later that during that same year patients with rhinoscleroma had been treated similarly and reports of it published in an obscure medical journal in Hungary. My patient was presented before this body some twenty years ago—a woman with rhinoscleroma of the nose which cleared up under treatment. I saw her five years later and she was still perfectly well. The obstruction had been so large that a rhinologist had to use an apparatus for permanently dilating the nostril to enable her to breathe through the nose.

A CASE FOR DIAGNOSIS: TUBERCULOUS GRANULOMA (?). Presented by DR. FRANK VERO.

F. J. H., a man aged *22*, born in the United States, gives a history of purplish areas developing on the right leg three years ago, which have increased in size. For the past three months he has noticed similar lesions on the left leg. There is no history of injury to the legs or previous eruptions of the skin or of any cutaneous disease in the family.

On the anterior surface of the right leg, extending from above the ankle to below the knee, are large, irregular, roundish, confluent, reddish-blue areas. The centers of the lesions appear somewhat yellowish and show telangiectases. The skin in the involved areas is relatively devoid of hair, and that at the centers seems to be slightly atrophic. On the lower third of the left leg is a similar patch about the size of a quarter.

The Wassermann reaction was negative. The reaction to tuberculin was slightly positive with a dilution of 1:1,000 and negative with a dilution of 1:10,000.

Biopsy led to a diagnosis of granulomatous tissue. The sections showed a slight atrophy of the epidermis, with a loss of rete pegs. The corium showed some evidence of fibrosis. The connective tissue cells were increased in number. There were both a diffuse and a focal perivascular infiltration by small mononuclear cells which had the appearance of lymphocytes. The walls of the blood vessels were thickened. Deep in the corium were collections which resembled epithelioid cells. These were seen among the sweat glands and about some of the vessels, frequently forming tubercle-like clumps. Here and there were giant cells. Small areas of necrosis were seen in the collagen.

DISCUSSION

DR. E. WILLIAM ABRAMOWITZ: My impression is that the eruption is the end-result of either a scleroderma or a sarcoid.

DR. LOUIS TULIPAN: I saw a patient presented by Drs. Zeisler and Caro before the Section on Dermatology of the American Medical Association, whose eruption resembled this one very much. The condition was called necrobiosis lipoidica diabeticorum, found in diabetic patients; it gives the picture of sclerodermatous patches with telangiectasia, slight brownish pigmentation and a central yellowish tinge. This patient presents several similar patches on the legs. The case I saw was the exact duplicate of this one, with the exception of the brownish pigmentation. It would be interesting in this case to ascertain the findings with regard to blood sugar.

DR. FRED WISE: Although the clinical appearance is that of scleroderma, the histologic observations seem to point to a tuberculoma, such as sarcoid. I am reminded of a case of clinical scleroderma of the legs in one of Dr. Fordyce's patients, in which the histologic examination revealed a leproma. I also saw the patient referred to by Dr. Tulipan, and agree with him that the lesions in this patient resemble those of necrobiosis lipoidica diabeticorum of Urbach and his co-workers.

DR. FRANK VERO: The patient was seen for the first time two months ago. He had noticed numerous round reddish-blue lesions on his right leg, which gradually became confluent. The clinical diagnosis at that time was scleroderma,

possibly in spontaneous involution. Against this diagnosis was the absence of induration, which is always pronounced on the lower part of the leg along the tibia. Many new lesions appeared recently on the lower part of the left leg which were only slightly infiltrated and were too soft for scleroderma. Dr. Cannon thought that a tuberculous condition or an atypical erythema induratum was possible. The blood was not examined, but urinalysis showed a negative reaction for sugar.

ERYTHEMA MULTIFORME BULLOSUM. Presented by DR. PAUL GROSS.

J. L., aged 23, born in the United States, states that the present eruption followed a severe sunburn which she acquired in August, 1933, while swimming in a pool. The eruption first appeared while she was still peeling from the sunburn; it started on the back and spread over the body, involving the face and lips.

Examination revealed on the face and lips, hands, arms, trunk and buttocks a vesiculobullous eruption accompanied by erythema. The bullae were tense and were filled with serous material. There was considerable crusting where bullae had ruptured. The remaining results of the physical examination were essentially negative.

The patient was hospitalized for twenty days. The temperature averaged 100 F. for the first week and then became normal. During the first week the lesions continued to spread and increased in size and severity, but gradually cleared as the temperature returned to normal. Following the patient's discharge from the hospital, some of the lesions on the extremities and trunk recurred.

Cultures from one of the bullous lesions showed no growth. The blood during the eruptive stage showed: hemoglobin, 100 per cent; red cells, 4,950,000; white cells, 11,800; polymorphonuclears, 76 per cent; lymphocytes, 12 per cent; mononuclears, 10 per cent, and eosinophils, 2 per cent.

DISCUSSION

DR. E. WILLIAM ABRAMOWITZ: I agree with the diagnosis, but the prognosis should be guarded. In view of the onset after exposure to the sun, the development of fever and other constitutional symptoms in the first attack and the tendency to recurrences since, it seems possible that ultimately a pemphigus or a disseminated bullous lupus erythematosus may develop. The patient should be watched carefully.

A CASE FOR DIAGNOSIS: NEVUS UNILATERALIS (?) LINEAR LICHEN PLANUS (?). Presented by DR. GEORGE B. ANDREWS.

F. P., aged 10, born in the United States, first noted his condition about one and a half years ago. On the anterior and lateral surfaces of the left thigh are irregularly shaped, partly annular lesions, purple-red, with numerous telangiectases. Although there is a close resemblance to angioma serpiginosum, the lesions have been proved clinically and histologically to be inflammatory.

A roentgenogram of the chest showed a slight peribronchial infiltration; the pulmonary fields were clear. There were a few moderately enlarged and partly calcified glands on both sides. Examination of the sinuses showed the frontal sinuses to be small and the antrums equal and clear. The tonsils are enlarged and infected.

Biopsy showed little change in the epidermis. There was a cone of intense edema with a dense infiltration chiefly by lymphocytes in the papillary layer of the corium. This suggested somewhat an infiltration by lymphoblastoma or possibly lichen planus. No diagnosis was made.

DISCUSSION

DR. SIGMUND POLLITZER: The lesions are limited to the front of the left thigh. Their shape and location suggest an artefact. I recommend that a careful inquiry be made from this point of view. The histologic changes as reported give no clue.

DR. WALTER JAMES HIGHMAN: The first thing one thinks of is an artefact, but the microscopic appearances negate such a hypothesis. I have an idea that a clue to this problem will be obtained only if it is possible to keep an eye on the patient for the next two or three years. It may be a rare form of telangiectasia of the skin, an atypical poikiloderma with changes going on in the corium. I think that Dr. Andrews may have found a unique type of dermatosis which undoubtedly, in European periodicals, would have a polysyllabic name.

DR. J. GARDNER HOPKINS: I do not think that the possibility of dermatitis artefacta was considered. The astonishing histologic changes could not be correlated with the clinical picture.

DARIER'S DISEASE. Presented by DR. G. A. MACHACEK for DR. J. GARDNER HOPKINS.

G. H., aged 20, white, an American, states that he has had this eruption for the past eight years. There has been no itching. There are discrete, brown, warty lesions in the antecubital regions and axillary folds. These lesions do not necessarily suggest follicular development. On the eyelids and on the chest are some definitely follicular papules and formations resembling comedones. On the back of each hand is a region made up of almost confluent wartlike lesions with a roughened surface.

A histologic diagnosis of keratosis follicularis (Darier's disease) was made. Numerous sections were cut from the specimen. The epidermal layer was thrown up into a papillary form with low projections. In general there was a moderate loose hyperkeratosis which followed the papillary outline. In places, however, rather thick hyperkeratotic masses were seen which seemed to depress the epidermis. Here one noted areas of parakeratosis and occasionally, in the underlying hyperplastic epithelium, swollen rounded epithelial cells which had undergone dyskeratosis. The epidermis in these locations showed a splitting which occurred just above the basal layer, and in the cavity so formed epithelial cells could be seen which had undergone dyskeratosis. Here and there in the epidermis was an occasional cell which had the character of the *corps ronds*. The superficial corium just beneath the epidermal sites of maximal pathologic change showed marked edema and chronic inflammation. The pathologic changes described seemed to be localized to the vicinity of the follicular funnels and outlets of sweat glands.

A CASE FOR DIAGNOSIS: DARIER'S DISEASE (?). Presented by DR. A. BENSON CANNON.

M. E., a white woman, aged 23, born in the United States, states that this disorder started on the trunk four and a half years ago and spread gradually. Two years later it involved the face. At times there was improvement, especially after exposure to the sun. The condition has been treated locally and also with injections, without benefit.

On the trunk is an erythematous and slightly scaly eruption consisting of infiltrated patches which prove on close inspection to consist of small nodules. Discrete nodules of the same type are found scattered over the trunk. In the right popliteal space is a bluish-red, infiltrated, linear, crusted lesion about 2 cm. in diameter. On the face, particularly over the area of flush of the cheeks and above the eyebrows, are reddish patches covered with greasy scales showing definite infiltration and formation of small papules.

A histologic diagnosis of keratosis pilaris was made. The sections showed marked hyperkeratosis and parakeratosis at the outlet of the duct of a sweat gland. Within this plug was a collection of nuclear material which appeared to be composed of polymorphonuclears. The plug had depressed the epidermis, which had undergone atrophy and degeneration. Edema of the epidermis and underlying corium was seen. A marked infiltration of both epidermis and corium had occurred. This infiltration was also present about the neighboring blood vessels. The cells were small, round and mononuclear, resembling lymphocytes. Some of the cells appeared to be polymorphonuclears.

DISCUSSION

DR. SIGMUND POLLITZER: While the first patient's disorder certainly bears some resemblance to Darier's disease, I am not convinced that it is that disease. In talking with Dr. Hopkins, who saw the sections, I learned that they do not directly suggest Darier's disease. There is a condition described by Kyrle which, perhaps, this resembles. I question the diagnosis of Darier's disease and I think that this might well be the condition described by Kyrle, which consists of horny papules penetrating the cutis.

DR. WALTER JAMES HIGHMAN: I do not doubt that the first patient has Darier's disease, but regarding the other patient I believe as Dr. Pollitzer does about the first patient. The histologic report is more than inconclusive; it does not remotely indicate that this is Darier's disease. My impression is that this is one of those unusual types of follicular seborrhea with a suitable name described by the French.

DR. MARION B. SULZBERGER: I agree with Dr. Pollitzer as regards the diagnosis in the case of the boy. I think that many of the characteristic localizations and lesions of Darier's disease are missing in the boy and present in the woman. I have seen several cases of the disease described by Kyrle. The full name is hyperkeratosis follicularis et perifollicularis in cutem penetrans. The histologic picture corresponds closely with that in the cases reported by Kyrle, and the clinical picture resembles to some degree the later (atypical) stages of the condition in the cases which I have seen recently.

DR. HERMANN GOLDENBERG: I accept the first case as one of Darier's disease. As regards the second case, I do not think that it is one either of Darier's disease or of Kyrle's disease. Is Kyrle's disease not localized in the axillae?

DR. J. GARDNER HOPKINS: In regard to the boy, I am particularly concerned as to treatment. The disease is in the early stage and the changes are as yet relatively slight. I hoped for suggestions as to the best method of treating the patient. If one can ever influence the course of this disease, it should be possible in the early stages, before profound changes have occurred.

As regards Dr. Cannon's case, I believe that he presented it with a question mark after the diagnosis. If the condition is not Darier's disease, what is it? I think that the second case is more interesting than the first. I am reminded by Dr. Machacek that the title of Kyrle's disease is hyperkeratosis parafollicularis et follicularis in cutem penetrans. The only striking lesion in this case is the keratotic plug in the sweat gland.

DR. MARION B. SULZBERGER: I do not remember Kyrle's exact clinical description. In the cases that I saw the lesions were not localized exclusively in the axillae, but were found on the neck and back, extending up into the scalp and well generalized on the trunk. In one case that I saw (reported by Bruno Bloch) there were even lesions of the mucous membrane. Although most of the lesions are follicular, I have seen many interfollicular lesions.

DR. FRED WISE: Replying to Dr. Hopkin's question: I have read several reports from reliable sources indicating favorable results in the treatment of Darier's disease with Grenz rays. In one case, that of a nurse from the Jamaica Hospital treated at the clinic of the New York Post-Graduate Medical School and Hospital, the lesions responded much more readily to Grenz rays than to any other remedy.

DR. PAUL GROSS: I saw the original case reported by Dr. Kyrle. The hyperkeratosis was much more pronounced. The lesions developed very rapidly and had remissions.

SYCOSIS VULGARIS: A NEW METHOD OF TREATMENT. Presented by DR. SAMUEL M. PECK and DR. LOUIS CHARGIN.

R. C., a man aged 33, has had sycosis vulgaris for ten years. He received a number of epilating doses of roentgen rays with resultant roentgen dermatitis.

He also had brilliant green therapy, with only temporary results. There were repeated recurrences of the condition. On Nov. 15, 1932, treatment with an ointment containing chlorhydroxyquinoline, benzoyl peroxide, eucalyptol and oil of thyme was started. In one month the face was clear of lesions. Regular use of the ointment is necessary to prevent recurrence. The patient had a typical sycosis vulgaris of the face over a background of roentgen dermatitis. The lesions were especially noticeable on the neck and on the sides of the chin, where there was no permanent loss of hair. The lesions were also seen on the forearms and thighs. The lesion on the right forearm has been allowed to recur in order to show what takes place when use of the ointment is discontinued.

SYCOSIS VULGARIS: A NEW METHOD OF TREATMENT. Presented by DR. SAMUEL M. PECK and DR. LOUIS CHARGIN.

H. P., a man, aged 30, has had sycosis vulgaris for five years. He had many epilating doses of roentgen rays with resulting roentgen dermatitis. He was also treated with brilliant green, arsphenamine and a sterile milk preparation. Physical examination showed typical sycosis vulgaris engrafted on skin changed by roentgen rays. Treatment with the ointment described in the preceding abstract was commenced on March 16, 1933. In one month the skin was clear. Prompt recurrence took place when the ointment was discontinued. The skin is now kept clear by regular use of the ointment.

SYCOSIS VULGARIS: A NEW METHOD OF TREATMENT. Presented by DR. SAMUEL M. PECK and DR. LOUIS CHARGIN.

M. S., aged 35, has had sycosis vulgaris for three years. He received twenty treatments with roentgen rays, with epilation. Physical examination revealed a typical sycosis vulgaris of the bearded area. Treatment of the lesions was begun on Feb. 2, 1933, with the ointment described above. The skin was clear on March 9. There is a prompt recurrence when use of the ointment is discontinued. The skin becomes clear again when treatment with the ointment is resumed.

SYCOSIS VULGARIS: A NEW METHOD OF TREATMENT. Presented by DR. SAMUEL M. PECK and DR. LOUIS CHARGIN.

A. Z., aged 62, has had sycosis vulgaris on his upper lip for five months. Physical examination revealed typical sycosis vulgaris. It was very refractory to ordinary treatment with salves. Treatment with an ointment containing benzoyl peroxide, eucalyptol and oil of thyme was begun on March 30, 1933, and was efficacious, the lesions clearing up in five weeks. The patient uses the ointment nightly.

SYCOSIS VULGARIS: A NEW METHOD OF THERAPY. Presented by DR. SAMUEL M. PECK and DR. LOUIS CHARGIN.

R. W., a man, aged 25, has sycosis vulgaris of the bearded area, arms and thighs. The patient is presented at the beginning of treatment; the ointment described in the preceding abstract has been used for about a week.

DISCUSSION

DR. SAMUEL M. PECK: During the past year we have treated about twenty patients with sycosis vulgaris and two with acne varioliformis, using a combination of antiseptics which were found efficacious. We found that it took from five to six weeks to clear up the condition in the majority of the cases, if the preparation was rubbed in twice a day. Many of the patients had had the disease for years and had received a great variety of treatments with roentgen rays, vaccines, foreign proteins, arsphenamine and other drugs. It is interesting to note that while the ointment without chlorhydroxyquinoline was effective, it was not so effective

as the ointment containing that substance. This is peculiar, since chlorhydroxyquinoline alone in twice the strength used in the ointment was not effective. This presents an interesting example of the synergistic action of drugs. If use of the ointment is discontinued even after complete clearance of all of the lesions, there is, in a majority of the cases, a prompt recurrence. This is seen after the ointment has been used for months. We suggest that sycosis vulgaris is not a contagious or infectious disease in the ordinary meaning of the term, but that it is an infection by ordinary staphylococci for which the terrain of the patient forms a perfect culture medium. By use of the ointment we render this culture medium (the skin of the patient) unsuitable for the growth and development of these organisms.

Since we have not made histologic studies in these cases, we are not prepared to state whether microscopically there might not still be evidence of the disease even when there is no clinical evidence of the lesions.

We have found it practical to simplify the treatment in continued employment of the ointment during the period of freedom from eruption. The patient should shave every day, rub the ointment into all of the parts involved and then wash it off after having allowed it to remain on for from ten to fifteen minutes. This obviates a constant greasy application. Strangely enough, we have had very little cutaneous irritation in our patients with sycosis vulgaris but have found that the ointment irritates the skin of patients with other conditions.

DR. MARION B. SULZBERGER: I compliment Dr. Peck and Dr. Chargin on the excellent results they have achieved in the treatment of sycosis vulgaris. It is unnecessary to expatiate on how resistant this disease is and how disagreeable the task of treating it. To get the patients to look as well as those shown here is an accomplishment.

DR. CHARLES LERNER: I should like to ask Dr. Peck whether he hesitates to administer superficial roentgen therapy in conjunction with the formula I. In other words, is formula I as irritating and as likely to produce erythema as a strong sulphur, salicylic acid or mercurial preparation.

DR. FRED WISE: Dr. Peck and Dr. Chargin are to be congratulated on the results thus far obtained in their treatment of sycosis barbae. The results have been so favorable that it is conceivable that ultimate cures may be achieved by a combination of their use of local remedies with other methods of treatment, such as mechanical depilation and the use of vaccines, bacteriophage and hot wet dressings. I assume that they have confined themselves thus far to local treatment in order to evaluate the remedy.

DR. ISIDORE ROSEN: I have seen the results of the work carried out with this new ointment in the clinic and think that Dr. Peck and Dr. Chargin are very modest in their presentation. Some of these patients were treated in other clinics for seven or eight years with all types of therapy, including roentgen rays and depilation, without results. It is well known how one reacts to the therapeutic possibilities when a patient suffering from sycosis vulgaris comes for consultation: one usually throws up one's hands because of the uniform failure in such cases.

DR. WALTER JAMES HIGHMAN: I think that the salient feature in Dr. Peck's work has been missed. Dr. Peck has not found a new antiseptic; he has not found any mysterious effect of certain agents that he has mentioned on an infective organism, but he has caused the skin to be converted into an unfavorable culture medium. This is a valuable addition to the management of recalcitrant cutaneous infections. I think that this is the point to be emphasized in appraising Dr. Peck's and Dr. Chargin's work. If that is true, all questions with reference to the application of Dr. Peck's ointment in combination with roentgen therapy and the like are irrelative. If his principle is sound, these other methods need not be considered. I wish to reemphasize that perhaps Dr. Peck has made an important contribution to the treatment of infections of the skin.

DR. E. WILLIAM ABRAMOWITZ: Through the kindness of Dr. Peck, I was able to obtain from a manufacturer some of this ointment for use with two patients. I found the preparation irritating; in fact, my patients refused to continue using

it. I saw little improvement during the few weeks that they applied it. One of the ingredients, benzoyl peroxide, is known to be highly explosive, and for that reason I believe that patients using it should be warned to keep away from fire. I shall attempt to use it again on other patients, as the results presented tonight warrant a further, extended trial.

DR. GEORGE B. ANDREWS: That the effects of the use of the ointment are temporary is probably due to the continued existence of infection within the hair follicles. In ringworm of the scalp one sees the same temporary response to ointments and a tendency to recurrence as soon as their use is stopped. I believe that epilation—either manual or by means of roentgen rays—might make the effects of the ointment more lasting.

DR. PAUL BECHET: The point Dr. Andrews brought up about epilation reminds me that I had under my care a patient who years ago consulted Dr. Wise for a generalized folliculitis. The patient was also treated by myself and many others, with indifferent results. After a lapse of years I saw him again, and to my surprise he was practically free from his intractable disease. He attributed this excellent result entirely to self-epilation which he had practiced almost daily for years.

Dr. Chargin and Dr. Peck are entitled to the warmest appreciation should the treatment prove as efficient in the hands of others as it has in theirs, and from the evidence submitted tonight there seems to be no reason why it should not.

DR. HERMAN GOODMAN: I am interested to know if Dr. Peck used his ointment minus any ingredient other than chlorhydroxyquinoline. Were the essential oils needed for the good effect? Would hydrous wool fat alone do what the ointment did? I can report excellent results in treating sycosis vulgaris by local intradermal injections of d'Herelle's bacteriophage. D'Herelle had not previously used the pyophage for local intradermal injection at the site of infection and called me from New Haven to learn if there were any ill effects.

More recently I have injected physiologic solution of sodium chloride locally into furuncles with good effect. Physiologic solution of sodium chloride has also been used in patients with pustular acne. I believe that its use in the treatment of infective processes of the skin has not previously been recorded, although it was recognized thirty years ago as valuable in postoperative shock.

DR. CHARLES LERNER: Apropos of what the previous speakers said, I should like to mention a case of obstinate sycosis vulgaris in a patient who came to me with radiation sequelae, and who was under my care for a considerable length of time; after I had tried almost everything in the pharmacopeia, the lesions, to my great surprise, completely cleared up after a severe attack of pneumonia.

DR. WALTER JAMES HIGHMAN: I think that there has been a good deal of tilting at windmills. Many of the windmills were indicated by Dr. Peck and Dr. Chargin. I, too, thought of brilliant green. There are many patients who recover in spite of therapy, as well as because of it. Dr. Peck's thesis was simple. He did not say that he had a "cure" for sycosis, but that he had an agent that rendered the skin unfavorable for the growth of stapylococci. The blatant fact is that dermatologists have tried everything there is to use in the treatment of sycosis vulgaris and nothing has worked. Dr. Peck's method seems to.

DR. MARION B. SULZBERGER: Skepticism is healthy. But to disbelieve blindly whatever is new is neither wise nor intelligent. I assume that the statements made by Dr. Peck and Dr. Chargin are correct. They state that they have treated over twenty consecutive patients suffering from sycosis vulgaris with this one method of treatment and have obtained uniformly excellent results. I have never seen equally beneficial effects in that number of consecutive cases through any other form of treatment. That, I think, is a step forward. It has always been thought, and there has been experimental evidence to prompt one to continue thinking, that the crux of the question of sycosis vulgaris relates to the altered resistance of the skin and follicles. The cocci which cause these lesions are appar-

ently identical with those which pullulate saprophytically on normal skins and in normal follicles. The patients with sycosis have locally lowered resistance to these micro-organisms.

Dr. Peck and Dr. Chargin state that they do not believe that they have been able to change this pathologically lowered resistance of the skin. For this reason the sycosis exacerbates as soon as the antiparasitic applications are discontinued.

Dr. Sigmund Pollitzer: The dismay experienced by the dermatologist when a patient with sycosis vulgaris comes into his office is well known. Through the kindness of Dr. Peck I have had a limited experience with this remedy. I have never seen such results from any other method of treatment. The patient's skin cleared up in about ten days and they have had no lesions since. The remedy was applied twice for a couple of weeks and once a day after that. The preparation discussed this evening certainly clears up sycosis. The patients need not care very much whether they are cured or not, so long as they can remain free from the eruption by using the ointment once a day.

Dr. Louis Tulipan: I treated one of the patients presented tonight for a year and a half and, I confess, without success. The patient received roentgen therapy and applications of brilliant green, gentian violet, ammoniated mercury and other preparations. At times the skin cleared up, and then in one or two weeks the condition recurred. This is the first time that I have seen the patient in about six months and I am really surprised at his condition. He tells me that he has been well for two and a half months. That is the longest period that he has remained well. There is something worth while in this remedy.

Dr. Louis Chargin: Every one is well aware of the difficulties encountered in treating this condition. No matter what type of therapy has heretofore been employed—whether local applications of ointments or lotions, local or general injections or the various types of physical therapy—the results have usually been most disappointing; perhaps not more than 5 per cent of patients were benefited.

Chlorhydroxyquinoline ointment is a remedy which produces a satisfactory result in nearly all cases. There is no question that one can control the process with the use of this ointment, even though a permanent cure is obtained in but few instances. Its great drawback is that it must be used even after the process has disappeared, in order to prevent recurrences. This apparently indicates that its favorable action is due to a change in the local conditions so that the causative factor cannot act.

Dr. J. Gardner Hopkins: Has Dr. Peck tried this ointment in the treatment of other superficial infections, in that of ringworm of the feet for example? Could it be used on the eyelid?

Dr. Samuel Peck: It is useless to argue too much at this time for or against the use of this ointment in the treatment of sycosis vulgaris. You have seen the results in the patients presented. A number of these patients have been treated by many of you in the various clinics in the city with results which certainly were not comparable to the results which we have obtained. Furthermore, we have treated twenty consecutive patients with this disease and we have obtained a good therapeutic result in every one of them. I have tried this ointment on patients with ringworm and I believe that it has certain therapeutic possibilities for that infection.

In answer to Dr. Sulzberger's question as to how I came to use chlorhydroxyquinoline, I will say that I had tried so many ointments in the treatment of patients with stubborn sycosis vulgaris that I was glad to be able to try a new one. For some reason chlorhydroxyquinoline alone is not effective, but it certainly adds to the therapeutic efficacy of the other substances.

We did not use roentgen therapy in combination with this treatment, because we found that it was unnecessary. I suggest that an interval of two weeks should intervene between the treatment with roentgen rays and the application of the ointment. We were not able to cure the chronic blepharitis that accompanied the sycosis, because of the marked irritation of the conjunctiva. In this regard I am

trying all sorts of substances that might have an antiseptic value, and I believe that I have one which is not irritating to the mucous membranes. I will report on it at another session.

Sabourraud has clearly demonstrated that in sycosis vulgaris there are characteristic areas of infection which are not necessarily limited to hair follicles. That is why roentgen rays are often ineffective.

URTICARIA PIGMENTOSA IN AN ADULT. Presented by DR. ADOLPH ROSTENBERG.

The patient, aged 22, married, the mother of three healthy children, states that her present trouble started in the summer of 1932 with an eruption of small "blisters" which lasted about three months and left the present pigmentation. The eruption was very itchy. About four months prior to presentation, another attack occurred, the lesions resembling mosquito bites. These lesions also left pigmentation.

A fairly large number of brownish-black macules are scattered over the trunk, each being from 1 to 4 cm. in diameter and irregular in shape. On friction, each macule readily urticates.

The Wassermann reaction of the blood was negative and the blood count was normal. A section of the skin showed a normal epidermis and a few deposits of pigment in the basal layer. In the corium were several areas in which mast cells appeared; some of these areas were perivascular.

NEVUS UNILATERALIS COMEDONICUS (NEVUS FOLLICULARIS KERATOSIS). Presented by DR. JESSE A. TOLMACH.

This girl, aged 4½, was seen at the Stuyvesant Square Hospital on Sept. 25, 1933. The cutaneous condition for which she is presented has been present since one week after birth. No other members of the family have been similarly affected. There is a bandlike patch on the right side of the neck, starting from a point about 1 inch (about 2.5 cm.) below the angle of the jaw and running posteriorly for about 3 inches (about 7.5 cm.) toward the right shoulder. In the patch there are many comedones ranging in size from that of a pinpoint to that of a pinhead. At the sites of the larger comedones the follicular openings appear to be retracted. There are a few hard, apparently cystic masses deep in the skin. One of the lesions in this patch has on several occasions become infected and is now in the process of resolution. None of the other follicular openings in the area involved show evidence of inflammation.

PSEUDOPELADE, WITH UNUSUAL MANIFESTATIONS; OR FOLLICULITIS DECALVANS. Presented by DR. PAUL GROSS.

E. W. B., a colored woman, aged 39, born in the British West Indies, has had folliculitis of the scalp for seven months. In the region of the vertex of the head there are irregularly shaped patches of complete alopecia and definite atrophy. The condition seems to be spreading peripherally by forming small, firm, follicular patches which are somewhat reddish, but is not evidently pustular. The Wassermann reaction was negative. Histologic examination showed the surface of the epithelium to be edematous. The follicular funnels were plugged with masses of keratin. The unique feature was the abscess about a hair follicle which contained a large hair and also a hair in direct contact with the inflammatory process. Numerous polymorphonuclears were seen and large mononuclear phagocytes containing polymorphonuclears and cellular débris. Giant cells, connective tissue cells and newly formed blood vessels were evident. A histologic diagnosis of folliculitis decalvans was made.

SEBOCYSTOMATOSIS OR STEATOMATOSIS. Presented by DR. LEWIS B. ROBINSON.

B. S., aged 33, white, states that twelve years prior to presentation she noticed around one breast a few small pimple-like lesions which gradually increased in size.

After that there was a gradual spread of these small lesions over the abdomen, chest, neck and arms. The lesions vary in size from that of a pinhead to almost the size of a pea, and are hard and rubberlike on pressure. Some of them when squeezed show a little sebaceous-like material. Apparently the condition is that of multiple sebaceous cysts. The report of the biopsy confirms this. Similar conditions have been described under the name of steatomatosis multiplex or sebocystomatosis of Gunther. Most of the cases have occurred in males. There are records of only two or three occurring in women.

The only possible etiologic factor disclosed in the physical examination was a low basal metabolic rate of minus 17. The patient was given thyroid therapy, and it is thought that there have been no new lesions since then. Previous to this lesions had been occurring rapidly.

Histologic examination of the skin showed little that was remarkable in the epidermis. The corium just beneath the epidermis was somewhat edematous and cellular, with a moderate perivascular chronic inflammation. The chief interest lay, however, in two cysts within the corium which were lined by stratified squamous epithelium. One was oval; the other had a curiously tortuous contour and contained portions of hair.

POIKILODERMA ATROPHICANS VASCULARE. Presented by DR. PAUL E. BECHET.

M. D., a woman, aged 42, states that the disease first made its appearance on the breasts twenty-two years ago. Within seven years, it spread to the trunk and arms. There has been little if any progress of the disease since then. Inspection shows that most of the skin of the arms and upper trunk is covered with a reticulated pigmentation, telangiectasia and punctate atrophic areas, giving the characteristic simulation of old roentgen dermatitis.

MERCURIC PIGMENTATION. Presented by DR. LOUIS CHARGIN.

M. F., a woman aged 38, married, was born in Russia. For more than a year she has suffered from a pigmentation of the face. For seventeen years she used a facial cream for the removal of freckles. The applications were made three or four times a week. The pigmentation is present over the entire face and ears and is rather uniform in distribution. The color might be compared to that of slate. The conjunctivae are not affected. The skin is smooth and there is no evidence of dermatitis. During a period of observation of several months, the condition has remained unchanged. The medical examination disclosed nothing of significance. Examination of the blood showed: bleeding time, one and one-half minutes; fragility of blood corpuscles, normal; coagulation time, four minutes; blood platelets, 330,000; hemoglobin, 90 per cent; white cells, 8,300; red blood cells, 5,340,000; polymorphonuclears, 50 per cent; lymphocytes, 39 per cent; eosinophils, 3 per cent; mononuclears, 1 per cent, and basophils, 1 per cent. Urinalysis revealed a faint trace of albumin but no evidence of mercury. The blood pressure was 130 systolic and 90 diastolic. Roentgen examination of the abdomen and kidneys showed them to be normal. There was no calculus. Histologic examination of a small piece of tissue taken from the forehead at the hairy border revealed some hyperkeratosis; in places the epidermis was reduced to only a few layers. There was evidence of intracellular edema, especially around the basal layer. The epidermal processes were flattened so that no papillary bodies were seen. There was a moderate amount of inflammatory reaction, especially near the area of edema, consisting of mononuclear cells and fibroblasts. Below the epidermis there seemed to be an amorphous granular deposit of pigment which was not intracellular. This had called forth no inflammatory reaction. Chemical examination of the facial cream used by the patient revealed the presence of large amounts of mercury.

DETROIT DERMATOLOGICAL SOCIETY

H. J. PARKHURST, M.D., *Reporter*

Regular Meeting, Oct. 17, 1933

HARTHER L. KEIM, M.D., *Presiding*

NEVOCARCINOMA OF THE LEFT THIGH. Presented by DR. ROLLIN H. STEVENS.

The patient, an Italian girl, aged 4½ years, was first observed in 1929, at the age of 4 months, with a tumor 10 cm. in diameter which involved the entire left thigh, the vulva and the lower left quadrant of the abdomen and extended to the right side of the abdomen. The left leg was swollen to twice the normal size. The lesion was dark purplish brown, the portion on the abdomen being purple, and it was growing rapidly. It had been present at birth as a small purplish lesion in the middle of the left thigh. A specimen was taken for biopsy, and the removal of the specimen was followed by severe bleeding due to the great vascularity of the lesion. The pathologist's report, on Oct. 30, 1929, was as follows: The epidermis is normal. In the cutis are several areas of nevus cells exhibiting marked anaplastic tendencies with the formation of spindle cells and no formation of alveoli or acini. Diagnosis: nevocarcinoma." High voltage roentgen therapy, with 200 kilovolts and copper filtration, was administered from Nov. 5 to 16, 1929, and again from Jan. 2 to 20, 1930.

No recurrence of the original condition can be found. However, there is shortening of the left femur, both in the neck and in the diaphysis, and also of the left tibia and fibula. This shortening was first noticed eighteen months ago. The child's development appeared to be otherwise normal. She walked at the age of 18 months. There was a small adenoma of the thyroid gland.

DISCUSSION

DR. ROLLIN H. STEVENS: Some demineralization is apparent in the roentgenograms. Undoubtedly the ovaries were destroyed by the irradiation, the parents having been warned of this before treatment was started. It would be interesting to study the results of this early sterilization as the child grows older.

DR. CHESTER A. DOTY: Was there any history of carcinoma in the family?

DR. ROLLIN H. STEVENS: No. It is difficult to say whether the process was carcinomatous at the outset.

PAPULONECROTIC TUBERCULID. Presented by DR. WILLIAM G. SAUNDERS.

Mrs. M. D., aged 25, stated that an uncle died of pulmonary tuberculosis in 1929, and that her child died of tuberculous meningitis in 1931 at the age of 3 years. About eighteen months before presentation, Mrs. M. D. began to have lesions on her elbows, which gradually spread to the forearms and to the knees and legs. There have been a few on the fingers. Each lesion lasts from six weeks to two or three months, changing from a papule to a pustule and finally leaving a pitted scar. There is an elevation of the temperature in the afternoons.

DISCUSSION

DR. ARTHUR E. SCHILLER: A number of nodules were definitely palpable on the lower posterior portion of the legs, and one was quite bluish. This suggested that there might also be early erythema induratum.

DR. WILLIAM G. SAUNDERS: The patient has active early pulmonary tuberculosis. Following Dr. Schiller's suggestion, sodium iodide was administered intravenously, with apparent benefit to the papulonecrotic lesions, but this was discontinued after the appearance of an iodide eruption.

LICHEN CHRONICUS SIMPLEX. Presented by DR. WILLIAM G. SAUNDERS.

G. P., a man, aged 37, born in Greece, stated that an eruption first appeared on his legs about eighteen months before presentation. Other parts of the body became involved. When he was first observed, about six months after the onset, the lesions were circumscribed, erythematous, scaly, pustular and extremely pruritic. Their size varied from that of a dime to that of a dollar. Following applications of ointment of ammoniated mercury, U. S. P., the pustular element disappeared, but the other lesions persisted, with some tendency to grouping.

DISCUSSION

DR. CLAUD W. BEHN: I do not agree with the diagnosis. I have seen several similar cases of industrial origin, due to cutting solutions. On involution the lesions presented this same peculiar glistening appearance, with an active border and a bluish center.

DR. ARTHUR E. SCHILLER: This patient formerly operated a drill press, using a soda solution. He has not worked for eight months, but during this period of unemployment he has had five outbreaks of lesions in sharply circumscribed areas. The lesions are erythematous at first, becoming vesicular and moist, and later crusted and brownish. As they fade, a shiny, thickened condition of the skin persists, until there is a recurrence in the same area.

DR. HOWARD J. PARKHURST: My first thought was of a possible pustular psoriasis, which, I believe, follows a course similar to that described by Dr. Schiller. The lesions are sharply circumscribed and symmetrical. The feet show clinical evidence of dermatophytosis, and it is possible also that this eruption may be a dermatophytid.

DR. HARTHER L. KEIM: Most of the nails were thickened, yellow and brittle. It remains to be proved whether that condition is associated with pustular psoriasis or with dermatophytosis. The involvement of the toe-nails might be due to a toxic process.

DR. JOHN A. HOOKEY: I can suggest no diagnosis, although I have seen four other cases which seemed to fit into the same group and followed the same course. Two occurred in women, one an office employee and the other a teacher. The other two patients were men: a stoker and a steel mill worker.

DR. ROBERT C. JAMIESON: I have also observed similar cases, and in one or two of them there was apparent recovery, at least temporarily. Foci of infection were usually found, and in those cases in which there was recovery dental foci were present. The recurrent outbreaks were of the acute vesicular type, as in this case, simulating dermatophytid. The focus of infection may be found in the teeth or elsewhere.

DR. LOREN W. SHAFFER: I agree with Dr. Jamieson's views.

DR. GEORGE VAN RHEE: I agree with Dr. Jamieson. I recall the case of a nurse who had periodic outbreaks on the hands and forearms every six to eight months. Examination was made for foci of infection and four dental abscesses were found. After these had been removed, the eruption disappeared, and it has not returned. I am now observing a similar case, of five months' duration, in a man. He had three outbreaks, and now the condition has improved about 50 per cent following the removal of infected teeth.

CHICAGO DERMATOLOGICAL SOCIETY

MAX S. WIEN, M.D., *Secretary*

Regular Meeting, Oct. 18, 1933

OLIVER S. ORMSBY, M.D., *President, in the Chair*

A CASE FOR DIAGNOSIS (ERYTHEMA?). Presented by DR. JAMES H. MITCHELL.

This woman has erythematous lesions on the cheeks which have been present for eight months. They appeared within a few hours after an injection of procaine hydrochloride for extraction of teeth. She spent some time in Billings Memorial Hospital, where she was told that the lesions were of no importance and that they might be due to injury to a nerve. I first saw her on Aug. 2, 1933.

The patient had taken Ex-Lax (said to contain phenolphthalein) and Edrolax. Large doses of phenolphthalein had no effect on the lesions, however, and Edrolax was also without effect. Injections of procaine hydrochloride were made into the skin of the thigh at different levels; there was no effect on the lesions or on the skin at the site of the injections. The patient was then given a series of injections of 1 Gm. of sodium thiosulphate every other day, with no apparent effect. On September 13, 0.02 Gm. of gold and sodium thiosulphate was given intravenously. That night rheumatoid pains developed which lasted for some time. However, the patient stated that she had had similar attacks. The temperature was 98 F., and the blood pressure, 118 systolic and 74 diastolic. The leukocyte count was 7,200. On October 7, the hands, elbows and knees were given one-half skin unit of roentgen radiation for the arthralgia, with apparent benefit. The temperature was 98.8 F., and the leukocyte count, 6,800. On October 14, marked acute erythema almost covered the cheeks, and there was a small area of erythema to the left of the bridge of the nose. Roentgenograms made by Dr. Hubeny showed that the teeth were normal. General examination gave negative results. The erythema is rapidly increasing.

DISCUSSION

DR. S. W. BECKER: I saw this patient some time ago, when she had lesions that were entirely different from those present today. She had practically no erythema but had small yellowish-brown macules. She said that the lesions followed the injection of procaine hydrochloride for removal of teeth, but I doubt the connection. My associates and I treated the lesions with a peeling paste, but this did not bring about improvement, although when the patient was last seen she presented pigmentation but not the intense erythema and scaling that are present now.

DR. O. H. FOERSTER: A number of years ago Matzenauer and Polland described a group of eruptions appearing on the face and elsewhere that were connected with dysmenorrhea. At first glance one thinks of this in connection with Dr. Mitchell's patient. Eruptions associated with dysmenorrhea or occurring at the menses frequently are due to phenolphthalein contained in laxative preparations taken with more or less regularity at those periods. I doubt that the connection between the injection of procaine hydrochloride and the occurrence of the lesions is other than incidental. Dr. Mitchell has investigated the influence of phenolphthalein thoroughly, and aside from calling attention to Matzenauer's clinical group I have no suggestions to offer.

DR. C. W. FINNERUD: I considered dysmenorrheic dermatitis. It is known, however, that lupus erythematosus can be precipitated by a number of factors, internal and external, and because of the configuration in this case I think that that diagnosis should be considered. I feel that the patient has an atypical erythematous lupus.

DR. J. H. MITCHELL: Just two conditions were considered here: a drug eruption due to phenolphthalein or to procaine hydrochloride and lupus erythematosus. There is no connection with menstruation. The resemblance to lupus erythematosus is obvious, but when one looks at the lesions carefully a pinhead-sized spot of pigmentation is evident in some of them. The scaling is not of the type seen in lupus erythematosus. With that diagnosis in mind, I gave the patient a small dose of gold and sodium thiosulphate, whereupon a severe arthralgia developed which persisted for two weeks. I may obtain a biopsy specimen, and I shall try to keep the patient under observation.

NOTE.—By October 23, the arthralgia had ceased. On October 25, the erythema was more pronounced and more extensive; the temperature was 97.6 F., and the leukocyte count, 8,800. An injection of 0.01 Gm. of gold and sodium thiosulphate (in a buffered solution) was given. No arthralgia or other systemic reaction occured. On October 28, the injection was repeated. The temperature was 98.4 F. On October 30, the patient felt exhausted; a nodule resembling those of erythema nodosum had developed on the right shin; the mouth and throat were normal, and the heart and the lungs were apparently so; the temperature was 99.2 F.; the leukocyte count was 9,800, and a blood culture in agar was negative. On November 1, the patient felt much better; the temperature was 98.8 F., and the leukocyte count, 5,800.

The patient was sent to the Presbyterian Hospital and stayed there for ten days, during which time the leukocyte count remained about 4,000 with approximately 60 per cent polymorphonuclears. Blood cultures were negative. A roentgenogram of the chest showed normal conditions. The basal metabolic rate was —4. A series of injections of 1 Gm. of sodium thiosulphate was given, together with intramuscular injections of liver extract. The erythema spread over the entire forehead and face, and small papular lesions appeared about the elbows and on the dorsa of the hands. All treatment but the administration of calcium gluconate and calcium was stopped, and the patient was discharged on November 10. Since then, the erythema has rapidly decreased, and the leukocyte count has increased.

A CASE FOR DIAGNOSIS (PERIADENITIS MUCOSA NECROTICA RECURRENS?). Presented by DR. F. E. SENEAR and DR. M. R. CARO.

O. B., a white man, aged 36, gives a history of recurrent attacks of ulcers in the mouth since childhood. During the early years the attacks appeared every few weeks, especially when he was constipated, and were rapidly relieved by catharsis. About four years ago the attacks became more severe. He was having dental work done at that time, and the work had to be stopped because of the ulcers. Since then the attacks have been more severe and more persistent, the mouth seldom being free from ulcers. Occasional attacks of herpes simplex on the lips have occurred. The present lesions appeared about six weeks ago.

The lesions began as hard, tender lumps which soon became tender ulcers. There are now several circumscribed, deep ulcers on the buccal mucosa, the inner surface of the lips, the sides of the tongue and the palate. They vary in size from that of a pea to that of a silver quarter; some are round, and others, polycyclic, and the base of each lesion is covered by a thick, loose, grayish membrane. There is marked pyorrhea. Several gold and amalgam fillings are present in the teeth, but none of them is adjacent to an ulcer. The uvula shows marked scarring.

Microscopic examination of a smear of material taken from an ulcer showed Vincent's spirilla and many gram-positive diplococci, but neither Bacillus crassus nor diphtheroid bacilli were found.

DISCUSSION

DR. J. H. MITCHELL: I have observed for some time a patient who has lesions on the right anterior portion of the hard palate. When first seen the lesions were much like those presented by this patient. My patient had had teeth extracted, and I made a biopsy but did not find any signs of a malignant process. He has

been kept in good condition and almost free from lesions for some time by means of simple applications of radiotherapy and of ultraviolet irradiation from the mercury vapor arc in quartz.

DR. UDO J. WILE: I am interested in the diagnosis suggested. The lesions are much larger than those that one associates with periadenitis mucosa necrotica recurrens. For want of a better name, I suppose that cases of this type must be discussed under that head. In many cases of this syndrome I have thought that the patient had mild sepsis and that the lesions on the mucosa were infarcts. In one case in which the lesions had resisted all other types of medication they cleared up entirely after the administration of arsphenamine. I think that bacteriologic examination of the lesions is of no value in indicating the etiologic factor. The mouth is so filled with bacteria, which take on added virulence and occur in greater numbers in the lesions, that one cannot look for much help unless the bacteria isolated are found in sections taken from deeper lesions.

DR. MAX S. WIEN: I agree with Dr. Wile that the lesions in the mouth in this case are larger than those usually seen in periadenitis mucosa necrotica recurrens. They resemble the oral lesions seen in the case reported by Dr. Perlstein and me (*J. A. M. A.* **98**:461 [Feb. 6] 1932). The clinical course and the development of the lesions conform to those of the entity described by Loblowitz and Sutton. In a case of this type that I saw last year positive reactions to scratch tests with coffee and wheat were obtained. The patient drank a great deal of coffee and ate many crackers. The eruption disappeared on the removal of these foods from the diet.

DR. HAMILTON MONTGOMERY: My associates and I have a patient under observation at present who has deep, necrotic ulcers in the mouth and who is definitely sensitive to ingested chicken. The clinical picture corresponds to that of periadenitis mucosa necrotica recurrens rather than to that of the ordinary superficial stomatitis.

DR. C. W. FINNERUD: For several years Dr. Ebert and I have had an opportunity to observe a patient of Dr. Ormsby's, a woman who at times has presented lesions probably larger than those shown by this patient; we have always considered the condition to be definitely periadenitis mucosa necrotica recurrens. The lesions have been classic in every way except that some have been very large.

DR. OLIVER S. ORMSBY: I think it is well worth recognition that there is a stomatitis which is exceedingly difficult to manage and which in certain cases will progress in spite of all kinds of treatment. In practically all the cases the lesions begin as nodules. These break down and leave ulcers, which commonly are painful. I have seen patients lose weight, undergo a reduction of the blood hemoglobin to as low as 30 per cent and be almost bedridden because they could not take food. That such a condition is not ordinary aphthous stomatitis is evident. In some cases it belongs in the category of sensitization phenomena and responds to treatment. In some of the less serious cases it responds to treatment within a few months, while in others it continues indefinitely. My associates and I have had more success with arsphenamine, probably, than with other therapeutic measures. One patient responded temporarily to arsphenamine and later improved under treatment with gold and sodium thiosulphate. I think she did best while treated with an antimony compound, but none of the therapeutic agents accomplished the desired result. We have used all the forms of local medication that have been recommended. Some of the ulcers are as large as a hazelnut. Occasionally the lesions resemble tuberculous ulcers, but tuberculosis has been ruled out in our case by microscopic examination. I feel that this form of stomatitis is well worth more study. It was first described by Loblowitz under the title "ulcus necroticum mucosae oris (chronische Apthen)" and later by Sutton as "periadenitis mucosa necrotica recurrens." It is a nodular disorder that is often inveterate.

DR. M. R. CARO: Clinically the case seems to be one of periadenitis mucosa necrotica recurrens. From the standpoint of etiology, the effect of a possible

galvanic current can be of only secondary importance, for there are no lesions adjacent to the dentures. We considered strongly a possible allergic basis for the disorder, and arrangements have been made for performing cutaneous tests.

ERYTHRODERMIA (BULLOUS, ICHTHYOSIFORM, CONGENITAL)? ICHTHYOSIS PLUS EPIDERMOLYSIS BULLOSA? Presented by DR. PAUL A. O'LEARY and DR. LOUIS A. BRUNSTING.

D. C. K., a boy, aged 2 years, is said to have had a dry, scaling skin with fairly generalized bullous involvement at the time of birth. Because of the history of syphilis in the father, the baby was treated with mercury rubs and intravenous injections of arsenic for one year. Tests of the blood of the father and mother were negative, and the Wassermann test of the blood and the results of an examination of the spinal fluid of the child at the age of 6 months were likewise negative. No reaction positive for syphilis has ever been reported.

The child was seen at the Mayo Clinic on July 19, 1933, at which time the skin of the entire body was dry and showed scaling and crusting. Over the ankles, heels, soles, hands and wrists there were pustular bullae and considerable denudation and secondary infection. There was a bleb on the left knee, and scars left by previous lesions were seen on both knees. The boy's father has thickened, dry palms and soles which crack in the winter.

The laboratory data, including the results of flocculation and Wassermann tests for syphilis and of urinalysis, were normal. The hemoglobin was 70 per cent, and the leukocytes numbered 9,900 per cubic millimeter of blood. The result of the Pels-Macht phytopharmacologic test was reported as 78 per cent by Dr. Pels.

DISCUSSION

DR. UDO J. WILE: I think that this child presents an interesting example of ichthyosiform erythrodermia. Attention has been called to the large bullae as an unusual feature. Such cases are not common. The thing that suggests itself to me in discussing this case is that one could well conceive of ichthyosiform erythrodermia associated with a moderate degree of epidermolysis. The bullae are in the sites of physiologic trauma. The original cases of ichthyosiform erythrodermia, as I recall, did not present vesiculation but presented essentially hyperkeratotic lesions on an inflammatory base; in many cases there was no history other than a familial history of a definite nevoid tendency, and it is not at all outside the realm of possibility that there might be a combination of the ichthyosiform erythrodermia and epidermolysis. I think that this might be demonstrated if sections of the regions in which the bullae occur were stained for elastic tissue.

DR. J. H. MITCHELL: I asked the mother about trauma. She said that the child crawls on his hands and knees and is constantly on his knees but that vesicles have never developed on the knees.

DR. HAMILTON MONTGOMERY: When the patient was first seen a few months ago, Dr. O'Leary and Dr. Brunsting raised the question of the association of epidermolysis bullosa with the ichthyosiform erythrodermia. The bullous lesions were much more prominent than they are at this time. Biopsy on a specimen taken from the thigh showed all the histopathologic features of ichthyosiform erythrodermia. There was imperfect formation of the granular layer, and a bulla was seen in that region at one edge of the section. The bulla was probably the result of degenerative changes of the cells of the stratum granulosum. The elastic tissue was not appreciably changed, and there was nothing in the histopathologic picture to suggest epidermolysis bullosa. In order to decide whether the latter condition is present, it would be necessary to make another biopsy, taking a specimen from the heel or the extensor surfaces of the hands, where this disease is more frequently seen. I think that the points Dr. Wile brought out were well made.

XANTHOMA TUBEROSUM MULTIPLEX AND AREOLAR XANTHOMA WITH ATROPHY. Presented by DR. S. W. BECKER and DR. M. E. OBERMAYER.

This woman, aged 54, states that yellowish nodules have been present in her skin for seven years. They appeared first on the elbows and were removed surgically but recurred six months later. About that time lesions began to appear in other locations. One year before admission to the hospital she was told that she had a trace of sugar in the urine.

On the elbows, the knuckles and the lateral aspects of the fingers there are large, yellowish nodules and some erythema. Over the extensor surfaces of the arms, the buttocks and the flexor surfaces of the thighs and legs there are discrete and confluent plaques with yellow, elevated borders and depressed, brownish, atrophic centers. Over the buttocks there are a few small, discrete nodules. The clinical appearance is that of a combination of xanthoma tuberosum multiplex and areolar xanthoma with atrophy, as pictured in Jadassohn's "Handbuch der Haut- und Geschlechtskrankheiten."

Examination of the urine at the time of admission showed a heavy trace of albumin and occasional granular casts but no reducing substance. A dextrose tolerance test showed a definite decrease in tolerance. The blood sugar during fasting was 120 mg. per hundred cubic centimeters; in one-half hour after the ingestion of dextrose it was 228 mg., and at the end of three hours, 218 mg. There was a trace of reducing substance in the urine at the beginning of the test, which became marked after three hours. The blood cholesterol was 486 mg. per hundred cubic centimeters.

The patient was placed on a diet of 670 calories daily, and in four weeks she had lost about 15 pounds (7 Kg.). The blood sugar during fasting at the last examination was 89 mg., and the cholesterol had been reduced to 271 mg.

Biopsy showed considerable fibrosis with a moderate number of xanthoma cells. The brown color in the centers of the annular lesions is due to the presence of hemosiderin in the histiocytes.

DISCUSSION

DR. UDO J. WILE: This patient shows, I think, a rather gratifying response to the reduction diet on which Dr. Becker has placed her. She volunteered the information that the lesions have receded very materially in the centers and that they are distinctly softer. One must not expect too much from any form of treatment directed toward the withdrawal of fat from the lesions now present on the extensor surfaces of the hands, knees and elbows. These lesions are distinctly fibrotic, and the fibrous nature of such lesions led the early observers to describe them as "xanthofibromas." Some are so definitely fibrotic that it is difficult to find any true xanthoma cells in them. They respond very slightly and very slowly to reduction in diet. Furthermore, the influence of a low maintenance diet is much more pronounced in the diabetic type of xanthoma, of which this patient's condition is not an example. I think that the blood sugar is rather high, but Dr. Becker agreed with me that she has not a true glycosuria. Some one suggested to me that this form of xanthoma may occur in very thin persons, and under those conditions it would be difficult to advise an extensive reduction in the diet. I do not think that point needs to be seriously considered, for the weight of a person is frequently an unsatisfactory index of his consumption of food. It has been frequently shown that there is no relation between the ingestion of fat and the fat metabolism. I think that this is an extremely interesting type of xanthoma, and I believe that if Dr. Becker can continue with the low diet without danger of acidosis many of the large fatty lesions will disappear.

LICHEN PLANUS-LIKE ERUPTION AND MELANOSIS FOLLOWING ANTISYPHILITIC THERAPY. Presented by DR. E. P. ZEISLER.

The patient, a Jewish tailor, aged 54, sought relief from abdominal discomfort six months ago and in the course of a routine examination was found to have secondary anemia, arteriosclerosis, emphysema, a pathologic condition of the large

bowel and a 2+ Wassermann and a 2+ Kahn reaction. Examination of the blood at that time showed the hemoglobin to be 45 per cent of normal, and the erythrocytes to be 4,300,000 per cubic millimeter. One of his sons was under treatment for congenital syphilis.

The patient was given mercury by mouth and later eight intravenous injections of neoarsphenamine and eight intramuscular injections, probably of bismuth, by his physician. After the third injection he complained of itching, and a generalized eruption appeared.

On admittance to the hospital in August, 1933, he had a generalized lichenoid eruption, with many lesions suggestive of lichen planus, and severe secondary anemia, with marked weakness and shortness of breath.

Examination of the blood showed: hemoglobin, 34 per cent; erythrocytes, 2,450,000; leukocytes, 11,800; polymorphonuclear neutrophils, 75 per cent; eosinophils, 1 per cent; lymphocytes, 20 per cent; monocytes, 4 per cent, and some polychromatophilia and achromia. There were enlarged glands in the groins and in the axillae, one of which was removed for histologic examination and showed an acute, nonspecific hyperplasia. A section of the skin was reported as showing chronic dermatitis.

The patient was given a transfusion of 400 cc. of blood, iron by mouth and a diet high in vitamins. He left the hospital several weeks later much improved. Since then he has received weekly injections of sodium thiosulphate, and the improvement has continued. He still shows a diffuse lichenoid eruption, with a residual melanosis involving the skin of almost the entire body.

DISCUSSION

DR. M. H. EBERT: It is interesting to note the various types of eruption that may be simulated by the conditions resulting from administration of arsenic to certain sensitive persons. My associates and I had under observation at Rush Medical College for a long time a woman with a marked lichen planus-like eruption with pronounced pigmentation which could be recalled by the administration of arsphenamine. In another case the eruption resembled lichen pilaris. In Dr. Zeisler's case the melanosis is marked, but the lichenoid lesions are not so marked as I presume they were previously.

DR. MAX S. WIEN: Such eruptions are most frequently seen after the administration of arsenic, but they occur also following injections of preparations of gold and of bismuth. About two years ago I presented a patient with an eruption similar to that shown by Dr. Zeisler's patient which followed an injection of a gold compound for lupus erythematosus.

DR. C. W. FINNERUD: Recently I saw a patient who had arsphenamine dermatitis following which a macular pigmentation persisted on the face. He had received about twelve injections each of neoarsphenamine and bismuth at the time the pigmentation developed, and I was at a loss to know whether it was due to the arsphenamine or to the bismuth and what localized it to the face. I presume it was due to the arsphenamine. Has any one information along this line?

DR. E. P. ZEISLER: I purposely refrained from incriminating either the arsphenamine or the bismuth in my case. The striking thing was the response of the patient to the transfusion. He was in poor condition before that, and since then sodium thiosulphate has brought about considerable improvement. In acute lichen planus I have found that the intravenous injection of sodium thiosulphate gives as good results as any treatment that I have used.

AMYLOIDOSIS (LOCALIZED, LICHEN) OF THE SKIN. Presented by DR. RUBEN NOMLAND and DR. F. V. PLUMMER.

This man, Polish, aged 53, states that his disorder has been present for twenty-three years. It began in the middle of the anterior surface of the right leg following a fracture, soon appeared on the left leg and has slowly spread. Considerable

pruritus is present, but except for mild asthma of ten years' duration his general health is good and a complete physical examination revealed nothing of importance.

A symmetrical eruption is present on the legs, extending from about 15 cm. below the knees to about 10 cm. above the ankles. It is most marked over the anterior outer aspects and involves about two thirds of the circumference, the posterior inner surfaces being free. On the outer sides of the legs there is a definite patch formation, consisting of slightly scaling, brown, markedly lichenified areas apparently made up of confluent papules. The elementary lesions on the backs and sides of the legs are discrete, being firm, brown and slightly scaling papules averaging from 2 to 3 mm. in diameter. The smallest lesion is a papule of similar appearance less than 1 mm. in diameter. Following roentgenotherapy the papules become translucent. The large, lichenified plaques measure approximately 20 by 10 cm.

Biopsy of a papule revealed a homogeneous material forming a lens-shaped mass in the papillary and subpapillary layers of the cutis. In some places this was in contact with the epidermis, and it was never widely separated from it. The mass contained many pigment-bearing cells, fewer cells resembling young connective tissue cells and a normal number of capillaries. The mass stained red with methyl violet and yellow with van Gieson's stain (positive stains for amyloid), but tests with iodine and sulphuric acid were negative. At the edge of the larger masses and in areas where small papules were beginning it could be seen that the amyloid was being laid down about the capillaries of the papillae. There was a minimal deposit of amyloid in the elastic connective tissue sheaths of all of the hair follicles, whether they were near or at a distance from an amyloid deposit in the skin. Aside from this the hair follicles were normal, as were the other adnexa. The elastic tissue was absent in the amyloid masses and also in the apparently normal papillae at a distance from the deposit. The epidermis over the amyloid deposits was atrophic but showed, marked hyperkeratosis. No inflammatory reaction was noted in any of numerous sections either near or at a distance from the amyloid masses. There was no amyloid in the deeper tissues.

The Bennhold test for generalized amyloidosis (the intravenous injection of 1.5 per cent congo red) was negative, showing loss of 16 per cent of the dye from the serum in one hour. However, the subcutaneous injection of about 1 cc. of 1.5 per cent congo red in the vicinity of the amyloid papules resulted in a selective red staining of the papules within twenty-four hours, and six weeks later amyloid papules as far as 10 cm. from the site of the subcutaneous injection remained definitely rose-red. No congo red was demonstrable in the sections of nodules from the other leg forty-eight hours after the intravenous injection of the dye.

DISCUSSION

DR. UDO J. WILE: I think that seeing this case was worth my trip to Chicago. All dermatologists have seen local amyloid degeneration without having the slightest suspicion that the condition was anything but hypertrophic lichen planus, or lichen simplex. I wonder whether Dr. Nomland or some one else can suggest any feature that indicates amyloidosis before biopsy is performed. The lesions are extremely like those of lichen planus or lichenoid dermatitis, and apparently amyloid degeneration in the skin can accompany different types of lesions. My associates and I have a patient with amyloid lesions on the tongue which present the classic appearance of being sclerosed; on biopsy, however, the condition was found to be definitely amyloidosis. I think that dermatologists have frequently overlooked such cases if there are many like this.

DR. E. P. ZEISLER: It may be interesting in this connection to recall that Dr. Lieberthal reported a case of lichen planus in which lesions were distributed in shin guard form. I am wondering whether lichen planus atrophicus might show amyloid changes after a period of years. I should like to ask Dr. Nomland whether amyloidosis is usually a primary or a secondary disease.

DR. S. W. BECKER: I had an opportunity to see a case of amyloidosis in Vienna in which the eruption looked a great deal like this one except that there was a yellowish, translucent appearance which is not present in this case, perhaps because of the treatment that this patient has received. The histologic section in the case in Vienna showed no thickening or infiltration but chiefly amyloid deposits.

DR. OLIVER S. ORMSBY: I am sorry that Dr. Michelson is not present, for he has worked on this subject and published a splendid paper. About four years ago we presented a report on amyloidosis before this society. Since that time several cases have been reported and now the condition is well recognized. In most of the cases the lesions resemble either lichen planus or lichen simplex chronicus. There are differences, however, that suggest that a microscopic examination be made, by which the nature of the disease is revealed. I do not believe that there are as yet enough positive clinical findings for one to identify the condition without microscopic study. Dr. Nomland's experimental study in this case resulted in valuable findings.

DR. M. H. EBERT: I think that Dr. Nomland should be congratulated on his modification of the congo red test. The use of the substance by local injection is an ingenious test for local amyloidosis.

DR. RUBEN NOMLAND: I think that localized amyloidosis should be suspected when one sees a patient with what seems to be a severe lichen simplex chronicus below the knees. One can prove whether there is localized amyloidosis in such a case rather easily by the injection of about 1 cc. of 1.5 per cent congo red, which will give the appearance shown in the specimen presented by selective staining of the amyloid papules. The normal skin will not take up the congo red. Replying to Dr. Zeisler's question concerning primary and secondary amyloidosis, this case is like most of those of the primary localized forms described by Koenigstein, Freudenthal and others. Freudenthal, however, described a secondary amyloidosis of the skin which occurs chiefly in old persons with senile warts, epitheliomas and similar conditions. In the case presented here the primary deposit of amyloid is about the capillaries of the papillary bodies. I tried methyl violet as a selective stain, but it had no effect. The papules originally were considerably more elevated than they are now, were brown and showed definite scaling. The translucent papule is a common but not a constant finding in localized amyloidosis.

ADENOMA SEBACEUM (FAMILIAL). Presented by DR. C. W. FINNERUD.

This woman and her 16 year old daughter have adenoma sebaceum. Three other children are similarly affected. The maternal grandmother and other maternal relatives in Poland have the same disorder, some of them having an associated nevus on the face or elsewhere.

DISCUSSION

DR. E. A. OLIVER: Has the mother received any treatment, or is the appearance now merely the result of natural involution? Her lesions are not nearly so aggravated as the daughter's.

DR. J. H. MITCHELL: Is this girl a sister of the patient presented several years ago?

DR. H. R. FOERSTER: The lesions of the elder sister are unusual in that they do not exhibit the yellowish color and telangiectatic markings characteristic of adenoma sebaceum and present in the lesions of the younger patient.

DR. UDO J. WILE: This is a most interesting family group, apparently presenting a nevoid disorder. I think that one is often prejudiced about a disease largely because early observers have associated it with certain features. One expects to find such features and frequently they are not present. The general conception of adenoma sebaceum is that a large proportion of the cases are found in imbeciles or persons of low mentality. Dr. Ormsby tells me that this girl is

mentally normal, and I think that the familial occurrence is the best evidence that the condition is nevoid.

DR. O. H. FOERSTER: It is of interest that adenoma sebaceum and the tuberous sclerosis sometimes associated with it both occur in structures derived from the ectoderm. In well marked cases progressive mental deterioration occurs eventually.

DR. C. W. FINNERUD: The mother states that her face formerly was redder, and I noticed that where the eruption is not present there seems to be some atrophy, which apparently is senile atrophy. The vessels apparently have become eliminated, and consequently there is less color than formerly. I think that the patient Dr. Nomland mentioned was definitely of low mentality. This girl seems to be rather bright. Many observers believe that the condition is nevoid because of the occasional association of adenoma sebaceum with Recklinghausen's disease and with other disorders that can definitely be considered nevoid.

PITYRIASIS RUBRA PILARIS. Presented by DR. S. W. BECKER and DR. M. E. OBERMAYER.

This woman, aged 23, first noticed dryness of the hands and face with swelling of the hands five months ago. In about two weeks the condition spread to other portions of the body, redness and scaling appearing at the same time. She used only sulphur and lard locally. She states that she had been well except that she had a "nervous breakdown" one year ago and that one fallopian tube and one ovary were removed at about that time.

Except for the condition of the skin, physical examination gave negative results. The Kolmer and Kahn reactions of the blood serum were negative. Urinalysis disclosed no abnormal conditions. The basal metabolic rate was —2 per cent.

The palms and soles are erythematous, thickened and scaly; the hands and arms are similarly involved. The nails are yellowed and thickened, with thickening of the nail beds. A diffuse erythematous eruption with marked hyperkeratosis and "branny" desquamation is present over the upper part of the thorax. On the abdomen discrete erythematous papules from 1 to 2 mm. in diameter are present about the hair follicles. The face and neck are not involved.

A specimen removed from the advancing border of a lesion on the abdomen showed a parakeratotic and hyperkeratotic stratum corneum with keratotic plugging of indentations in the epidermis. The stratum granulosum was irregular and in some areas absent. The stratum mucosum was irregularly thickened and thinned between the prominent rete processes, which were clubbed. The papillary layer contained a moderate infiltration of round cells and plasma cells, largely perivascular.

PITYRIASIS RUBRA OF HEBRA. Presented by DR. M. H. EBERT and DR. MAX WOLF.

This girl, aged 6½ years, presents an eruption which has appeared gradually during the past six months and has caused no discomfort. She is underweight but otherwise appears to be well. There is no history of a hereditary predisposition to any disease of the skin.

On the legs well defined hyperkeratotic, scaling areas extend from the knees to the ankles and then externally almost around the ankle. The symmetry is remarkable. The scaling is most marked over the Achilles tendons and the external malleoli. The elbows and knees are moderately involved, and the palms markedly so. There is mild pityriasic scaling on the ends of the toes and fingers, on the lobes of the ears and in a few scattered areas on the face. The scalp is free, and no plugs are noted on the phalanges. On closer examination of the palms and elbows, the lesions seem to be made up of closely crowded, polygonal, flat-topped papules with keratotic scaling, and in places there is a suggestion of keratotic plugs.

Biopsy on a specimen removed from the margin of a lesion on the elbow showed thickening of the whole epidermis. There was well-marked hyperkeratosis with one or two small bands of parakeratosis. There was marked keratotic plugging of the follicular openings as well as moderate dilatation of the papillary and reticular blood vessels, with a moderate perivascular infiltration by lymphocytes and connective tissue cells. The elastic tissue was unchanged. The stratum granulosum varied in thickness and in a few places was absent. The rete pegs were longer and broader than they are normally.

DISCUSSION

DR. E. P. ZEISLER: I think that both Dr. Becker's patient and Dr. Ebert's have pityriasis rubra pilaris. They show the psoriasiform type of lesions often seen in children. Dr. Becker's patient presents a marked involvement of tissues under the nails as well as of the palms and soles. The child that Dr. Ebert showed does not have marked involvement of the nails, but I think that she has a mild type of the disorder. It would be interesting to see what could be accomplished with organotherapy in Dr. Becker's patient. I understand she has had nothing but local treatment.

DR. HAMILTON MONTGOMERY: Sweating induced by pilocarpine is sometimes of marked benefit in these cases.

DR. RUBEN NOMLAND: I wish to suggest regarding Dr. Ebert's case that the condition may be not pityriasis rubra pilaris but a congenital type of keratoderma with hyperkeratosis of the palms and soles and that it may possibly fall into the ichthyosis group.

DR. HAMILTON MONTGOMERY: There was nothing in the histopathologic picture to suggest ichthyosis; the changes were those characteristic of pityriasis rubra pilaris.

DR. M. H. EBERT: In regard to Dr. Montgomery's suggestion that there is not as much inflammatory reaction as is commonly seen, I wish to state that the biopsy specimen was taken from an early lesion and I understand that in the early stages the inflammatory reaction is not so marked.

EPITHELIOMA (MULTIPLE). Presented by DR. M. H. EBERT and DR. B. B. BEESON.

This man, aged 36, has a very low intelligence quotient, and the history is unreliable. As nearly as can be determined, the lesions appeared between one and two years ago.

He presents multiple lesions on the face, neck, trunk and arms. On the face there are several ulcers varying in size from that of a pea to that of a dime, involving chiefly the lower eyelids, nose and temples. The ulcers have largely destroyed the lateral two thirds of each lower lid, but there is no apparent injury to the eyes themselves. There is considerable eversion of the margins of the lids. The ulcers on the face show an irregular outline, with rolled borders and depressed, granulating centers, some showing central healing with scar formation. On the right wrist there is a firm, fungating, papillomatous lesion somewhat larger than a silver dollar. On the right side of the neck there is an ulcerated area 5 cm. in diameter, sharply demarcated and deeply punched out, with a firm, rolled edge. On the trunk are several scattered superficial, scaly, crusting patches. Many of the lesions are circinate, and all have threadlike, pearly borders.

Biopsy revealed: (1) in tissue from a lesion on the arm, a typical basal cell carcinoma; (2) in tissue from a lesion on the lower eyelid, a hornifying squamous cell carcinoma, and (3) in tissue from the lesion on the neck, a cylindromatous basal cell carcinoma of transitional to squamous cell type.

DISCUSSION

DR. HAMILTON MONTGOMERY: I agree with the clinical and pathologic diagnoses as presented. One lesion was a basal cell epithelioma; another, a basal squamous cell epithelioma, and still another, a squamous cell epithelioma of grade 1. I have seen a solitary epithelioma develop in a patient as young as 5 or 6 years. Although this patient presents multiple epitheliomas, the condition should not be confused with superficial epitheliomatosis (Ormsby). It is difficult to explain why a person so young should have multiple epitheliomas. There is no evidence of arsenical keratoses or of pigmentation. I understand that the patient's intelligence quotient is very low, so that it is impossible to obtain from him an accurate history of any occupational factors as precipitating agents.

DR. C. W. FINNERUD: The case is interesting because of the mixture of lesions of different types. I know that all those who saw the young man whom I presented at the clinical meeting of the American Dermatological Association in June, 1933, will be glad of a word about him. He had about a dozen nodules on the left arm and the left side of the chest, some with depressed centers, which resembled basal cell epitheliomas; there was a similar lesion on the margin of the left upper eyelid. The members were not able to arrive at a definite diagnosis but considered various types of tumors, including sarcomas and epitheliomas, as well as dermatitis factitia and dermatitis nodularis necrotica. The patient went to Rochester, where Dr. Montgomery examined serial sections and was able to prove the condition to be definitely epithelioma of grade 4. Since then the patient has had a radical amputation of the left arm and shoulder.

DR. HAMILTON MONTGOMERY: The patient referred to by Dr. Finnerud was recently at the Mayo Clinic. Biopsy revealed a squamous cell epithelioma of grade 4. The patient had chronic bronchiectasis, and several roentgenograms of the chest showed fairly discrete shadows which could be interpreted as bronchiectatic or as representing early metastatic nodules. We felt that the patient should be given the benefit of the doubt, however, and a complete amputation of the arm, including the shoulder joint, was done. The epithelioma of the eyelid responded very quickly to treatment with radium. It was probably, therefore, a basal cell epithelioma and independent of the other lesions. I have seen two or three patients with similar conditions who had multiple shallow epitheliomatous ulcers that spread along the lymphatics as melanomas do and invaded the internal organs only after a considerable time. The lesions have all been squamous cell epitheliomas of grade 3 or 4.

SYPHILIS (TERTIARY). Presented by DR. MAX S. WIEN and DR. MINNIE O. PERLSTEIN.

This man, aged 43, was operated on four years ago for a right inguinal hernia. Six months later the wound opened, leaving an ulcerated area which has healed and opened repeatedly. During the past year the lesion has enlarged and involved both the inguinal areas, and there has been a gradual enlargement of the scrotum. At the onset of the condition multiple draining sinuses were present in the scrotum, but these have healed. Three years ago, on admission to the hospital, the condition was diagnosed as tuberculous epididymitis and tuberculous lymphadenitis. About seven months ago he noticed the appearance of a hard lump in the left side of the neck, which began to suppurate three months ago. He was again admitted to the hospital on Sept. 20, 1933. Severe hoarseness had been present for a week prior to his admission.

The patient shows a superficial, symmetrical, nodular, ulcerative involvement of the crural, suprapubic and perineal areas. The lesions consist of thin, atrophic, wrinkled scars with sharp borders that have a tendency to form elliptic segments. The greatest activity is present at the periphery where, sharply demarcated from the normal skin in a more or less serpiginous fashion, there is a bandlike plateau of reddish-brown, infiltrated dermatitis, interspersed through which are punched-out ulcers and superficial adherent crusts varying in size from that of a pea to

that of a bean. An associated hydrocele and enlargement of the testes, especially the left, are to be noted. No subjective symptoms are associated with the eruption except a mild painful sensation on extreme pressure on the testes.

On the neck are discrete, grouped, reddish-brown nodules with some grooving of the skin in the center, giving rise to a crusted sulcus.

A laryngologist reported diffuse thickening of both arytenoid muscles and of the left vocal cord, which may be tuberculous. Examination of the chest shows no evidence of tuberculosis, and members of the staff in the department of tuberculosis do not agree with the diagnosis of tuberculous laryngitis. The roentgenograms and the sputum are negative for tuberculosis.

The result of a serologic test for syphilis in 1931 was reported as plus-minus; another test in 1933 was reported as negative.

A biopsy in 1931 was reported to have shown tuberculous granulation tissue. A recent one was said to have shown underlying tuberculous granulation tissue containing Langhans' giant cells and tubercles.

DISCUSSION

DR. L. F. WEBER: Has the patient had any antisyphilitic therapy?

DR. MAX S. WIEN: He was given mercurial inunctions for one week.

DR. M. E. OBERMAYER: The condition, I think, has all the earmarks of tertiary syphilis but not of tuberculosis. Since the results of biopsy are not conclusive, I feel that syphilis can be ruled out only by an extensive therapeutic test.

DR. HAMILTON MONTGOMERY: I think that clinically the case is one of tertiary syphilis, and the histopathologic observations are not against such a diagnosis. One should be very careful in making a diagnosis of tuberculosis of the skin merely because there are some giant cells of the Langhans type. In these sections there is no tubercle formation with the ordinary arrangement of epithelioid cells and giant cells. Instead, there are a few scattered irregular groups of epithelioid cells, and most of the giant cells present are of the foreign body type. Gans has emphasized that in differentiating between tuberculosis and tertiary syphilis it is important to include the margin of the lesion in the specimen for biopsy because at the margin the typical syphilitic involvement of the endothelium of the smaller vessels and the plasma cell infiltration about them are usually present.

DR. C. W. FINNERUD: The peripheral and the deep vessels, so far as could be ascertained in the sections, resemble more those seen in syphilis than those seen in tuberculosis, and the character of the infiltrate at least leans toward that side. I think it is more likely that the condition is syphilis.

DR. O. H. FOERSTER: I think it is syphilis of a rapidly extending, ulcerative type.

DR. MAX S. WIEN: This patient was seen in the hospital three years ago with a tumor of the testicle and draining sinuses in the scrotum. At that time the reaction of the blood serum was plus-minus; there were no other cutaneous lesions, and the condition clinically could be either tuberculosis or syphilis. The patient left the hospital before a therapeutic test could be instituted and was next seen two weeks ago with new cutaneous lesions symmetrically involving the groins and the suprapubic region, as shown today. This eruption is clinically tertiary syphilis. The grouped nodules in the neck have developed during the past six months, and it is a question whether they are a part of the same process. In order not to change the appearance of the skin previous to this meeting we have given only mild antisyphilitic treatment with mercurial inunctions. I feel that there has been some resolution even under this mild therapy.

NOTE.—Biopsy on one of the nodules in the neck revealed the microscopic changes produced by syphilis. On reexamination of the sections of the lesions on the scrotum and the groins the pathologist agreed that in the light of the clinical picture the microscopic changes are syphilitic.

LICHEN PLANUS. Presented by DR. M. R. CARO and DR. H. C. SCHORR.

This man, aged 47, from the Mandel Clinic, states that pruritic lesions on the skin of the forearms and burning of the lips developed about seven months ago, soon after he was beaten during a hold-up. Since that time the lesions have spread. The ones on the forearms are tender to pressure, and the pruritus has been intense.

On the extensor surfaces of the forearms and the sides of the neck are several large, circumscribed, violaceous-red, infiltrated patches. Those on the neck are covered by a thin, dry scale, and those on the forearms, by a thick, silvery, psoriasiform scale. On the dorsa of the hands and scattered over the forearms and feet are many annular, and a few angular, violaceous, lichenoid papules. The dorsum of the nose is covered by a large, dull red, circumscribed patch over which is a thin, dry scale, and similar but smaller lesions are scattered over the face. The lesion on the nose is improving under the oral administration of solution of potassium arsenite. Lesions are present on the vermilion borders of the lips, and there is extensive involvement of the palate and of the buccal mucosa.

Histologic examination of a specimen taken from the psoriasiform patch on the forearm showed a thick, non-nucleated scale, flattening of the epidermis, disorganization of the basal layer, edematous subepidermal lacunae and a dense subepidermal infiltration composed largely of lymphocytes and chromatophores.

DISCUSSION

DR. HAMILTON MONTGOMERY: I believe that the condition clinically and histopathologically is a generalized discoid lupus erythematosus histologically indistinguishable from subacute lupus erythematosus. Clinically the case is similar to one presented at the annual meeting of the Minnesota Dermatological Society in June, 1926, in the discussion of which Dr. Ormsby called attention to the presence of lesions like those of lichen planus. In that instance I held out a long time for the diagnosis of lichen planus because of the histopathologic changes. As a result of further study, however, I believe that the histopathologic picture of subacute lupus erythematosus and that of lichen planus can usually be differentiated. The sections in the case presented today show more marked atrophy of the epidermis than is usually seen in lichen planus, and also more edema of the lymphatics and more marked liquefaction necrosis of the basal cell layer. Furthermore, the infiltration is not sharply limited to the upper cutis but extends down along the blood vessels to the corium. If elastic tissue stains were available, they would show more marked destruction of the elastic tissue than is seen in lichen planus.

DR. H. R. FOERSTER: I believe that the clinical features favor a diagnosis of subacute lupus erythematosus disseminatus. The predilection of the lesions for the extensor surfaces of the forearms and the V area of the upper part of the chest and the edematous character of the papules on the chest speak against a diagnosis of lichen planus. The lesions of the mucous membranes were difficult for me to interpret, but I believe they fit into the picture of lupus erythematosus.

DR. E. P. ZEISLER: I had an opportunity to see this patient about a month ago and took some photographs. At that time he had much more marked erythema in a butterfly arrangement across the nose, and I remarked that one never sees that in lichen planus. The rest of the picture was the same as it is now. At that time I suspected lupus erythematosus rather than lichen planus, and I was surprised when Dr. Caro said that the histologic changes were those of lichen planus.

DR. E. A. OLIVER: The mucous membranes of this patient are distinctive. I have under observation a patient with lupus erythematosus of the mucous membranes only and two patients with lichen planus of the buccal mucosa, and the lesions in the mouth of this patient, I believe, are those of lupus erythematosus. The lesions on the dorsa of the hands have somewhat the appearance of lichen planus, but the remainder of the picture is that of lupus erythematosus.

DR. C. W. FINNERUD: I have observed several cases of this type and I have concluded that when the condition resembles both lupus erythematosus and lichen

planus it is lupus erythematosus. When it is borderline clinically it is usually borderline histologically. Atrophy of the epidermis is present in both diseases, but, as Dr. Montgomery brought out, the infiltrate is not so marked in lupus erythematosus. The lesions of the mucous membranes offer a great deal of help. Both types of lesions of lupus erythematosus are present on the buccal mucous membrane of this patient.

DR. M. R. CARO: When first seen the patient presented three types of lesions. The lesion on the nose strongly suggested lupus erythematosus; the lesions on the hands were typical of lichen planus, and there were psoriasiform patches on the extensor surfaces of the forearms. The histologic changes, while not those ordinarily seen in a typical lichen planus papule, were nevertheless not inconsistent with lichen planus. It seemed to us that the cutaneous lesions, the oral involvement and the histologic changes justified presenting this case as one of atypical lichen planus. In view of the opinions expressed, however, favoring the diagnosis of lupus erythematosus we are forced to accept this diagnosis.

A CASE FOR DIAGNOSIS (CHRONIC HERPETIFORM ERUPTION). Presented by DR. S. W. BECKER and DR. M. E. OBERMAYER.

This man, aged 24, single, born in Iowa, a guide at the Century of Progress, was first seen in the outpatient department of a hospital on October 5, complaining of a burning and itching eruption in one area on the back. He stated that the eruption had been present intermittently for ten months. The lesions tended to recur at shorter intervals, and they always recurred within the same area. The attacks were initiated by violent burning and pruritus; the patient then observed and felt one or more "bumps" about the size of a finger nail which were raised above the level of the skin, firm to the touch and bright red. Most of the lesions increased in size by peripheral extension, and some reached the size of a child's palm. Evolution of the lesions took place in about one week, and involution required only three or four days. The patient never wore suspenders, and he had not purchased new underwear previous to the appearance of the eruption. For six or eight years he had taken bromoseltzer every three or four months, but he had taken none since June, 1933. A proprietary preparation called Pepso-Bismol was taken several times a month from September to December, 1932. A powdered bismuth compound prescribed by a physician was taken about once a week after 1929 for chronic diarrhea, but the regular intake of this drug was stopped in September, 1932, and since that time he had taken it only once or twice.

Examination at the time of admission showed on the skin of the lower part of the back areas of erythema and of urticarial lesions alternating with areas of normal skin and of skin with definite hyperpigmentation. The Wassermann and Kahn reactions were negative. Examination of the blood showed: hemoglobin, 92 per cent; erythrocytes, 4,730,000; leukocytes, 8,200; polymorphonuclear neutrophils, 52 per cent; large lymphocytes, 29 per cent; small lymphocytes, 9 per cent; mononuclears, 8 per cent; eosinophils, 2 per cent, and no basophils. The urine was normal. When the patient was examined a second time, on October 12, small groups of vesicles could be seen on the areas which at the time of the first examination showed urticarial lesions.

Biopsy showed that the stratum corneum was loose and flaky. There was some parakeratosis all along the epidermis. The stratum granulosum was definitely thinned or absent. The stratum mucosum showed intercellular and some intracellular edema. There were prominent microscopic vesicles in this area, which contained serum and polymorphonuclear and eosinophilic leukocytes. A number of mitotic figures were present in the basal layer. The papillary region contained an infiltration of small round cells and polymorphonuclear and eosinophilic cells.

DISCUSSION

DR. H. R. FOERSTER: In commenting on this case Dr. Wile said that he had recently observed a similar condition in a patient in whom the histologic features

of Hodgkin's disease subsequently developed in a cervical lymph node. I understood him to infer that cutaneous Hodgkin's disease was to be thought of in this case. The lesion considered by itself suggested to me the possibility of Duhring's disease, and I should like to inquire whether that disease may exhibit a solitary lesion for as long a time as this condition has been present.

DR. L. M. WIEDER: I think that one should consider the possibility of injury to a nerve with recurrent lesions of herpetiform type in the area supplied. While the eruption extends rather far to the right it does not extend beyond the conceivable limit of overlapping fibers of the midline.

DR. HAMILTON MONTGOMERY: The sections show the histopathologic picture of a herpetic lesion and present none of the features of any of the lymphoblastomas. Dr. Wile's suggestion, however, is good. My associates and I have had several patients with lymphoblastoma, especially in the form of lymphosarcoma, in whom a single lesion on the back appeared first, followed by a group of satellite lesions. I recently saw a patient who presented an eruption similar to that in Dr. Becker's patient except that the lesions were urticarial rather than herpetic. Biopsy revealed lymphosarcoma.

DR. L. M. WIEDER: While I am on the subject of lymphoblastoma, I wish to state, with no relation to this case, that the patient with generalized erythrodermia whom I presented before this group several months ago, who had been studied by Dr. Foerster and me for several years, has since shown in the peripheral blood definite evidence of lymphatic leukemia, and has marked generalized enlargement of the lymph glands.

DR. S. W. BECKER: In studying this patient we have ruled out most of the simple conditions and have made a diagnosis of localized dermatitis herpetiformis. The patient has burning such as occurs in that disorder, and the histologic picture is compatible with that diagnosis.

Dr. Wile stated in regard to his cases that in the sections there was an infiltration by Dorothy Reed cells. The infiltration in our case is very slight, and there is no suggestion of lymphoblastoma. We are going to have the patient examined by a neurologist to see whether there is any involvement of the nerves and will have a roentgenologic examination made.

A CASE FOR DIAGNOSIS (SCURVY?) Presented by DR. MAX S. WIEN and DR. MINNIE O. PERLSTEIN.

This man, aged 70, entered the hospital complaining of severe pain in the legs of two weeks' duration, associated with discoloration of the skin of the legs. He stated that there was bleeding from the rectum following defecation and that he had occasional attacks of hemoptysis and night sweats.

The essential findings on examination were diffuse ecchymosis and purpura of the lower part of the legs, extending from the ankle to the knee, with sharp margination at the distal end. The same condition was present on the arms but to a lesser extent. The gums were swollen and hemorrhagic and bled easily.

Some improvement has occurred on a diet high in vitamins.

DISCUSSION

DR. O. H. FOERSTER: The edematous, bruised and corpselike appearance of the right leg is very suggestive of scurvy. I have seen several instances of scurvy in persons whose social status was better than the average and in whom one would not expect scurvy to occur. Several of the patients were elderly single women who cooked for themselves and lived very cheaply; subperiosteal hemorrhages, edema and the usual changes in the mucous membranes developed.

DR. MAX S. WIEN: This patient has been observed in the medical service, and some discussion arose in that department as to whether the condition should be diagnosed as pellagra or as scurvy. We saw him for the first time last

week and were impressed by the spongy gums, the anemia and the lesions on the lower extremities. Today these lesions are fading brown spots. We felt that the condition was scurvy.

A Case for Diagnosis (Kaposi's Sarcoma?). Presented by Dr. M. H. Ebert.

This woman, an Italian, aged 64, states that her disorder has been present for from six to eight months and that the lesions began on the left ankle as small "bumps" which gradually increased in number and size. She has lost about 20 pounds (9 Kg.) during the past six months. She complains of burning and aching.

Examination revealed a group of bluish-red nodules, varying in size from that of a pea to that of a walnut, on the medial aspect of the left ankle. Most of the lesions were round, firm and tender to pressure. Some of the larger nodules were ulcerated on the top and bled easily. Several firm, subcutaneous nodules were palpable along the medial aspect of the lower half of the leg, and there was one nodule on the anterior aspect of the leg just above the ankle. Varicose veins were present in both legs.

DISCUSSION

Dr. E. P. Zeisler: I favor the diagnosis of melanocarcinoma.

Dr. S. W. Becker: I think that the lesions are malignant growths, but I hesitate to classify them. I think that they are in the sarcoma group.

Dr. Hamilton Montgomery: I favor the diagnosis of Kaposi's sarcoma. The unilateral distribution does not negate such a diagnosis. Some of the lesions have hemorrhagic characteristics, and it seems rather unlikely that melanoma would have so many discrete, localized lesions without more evidence of extension along the lymphatics. I think that the diagnosis must rest on the histopathologic picture.

Dr. H. R. Foerster: I agree with the opinion expressed by Dr. Montgomery.

Dr. E. A. Oliver: I believe that the condition probably falls in the sarcoma group but that mycosis fungoides d'emblée should be considered.

Dr. M. R. Caro: I think that this is malignant melanoma. Since such a tumor is derived from nevus cells and merely simulates the histologic structure of epithelial or connective tissue tumors, it is not possible to classify it as melanocarcinoma or as melanosarcoma.

Dr. Oliver S. Ormsby: Kaposi's sarcoma is rather rare, but each case presents abundant opportunity for the study of the condition. I have observed several cases in a number of years, but none has presented the picture exhibited in this one. Kaposi's idiopathic multiple pigmented sarcoma is characterized by nodules and plaques which usually are symmetrical. It commonly begins on the dorsa of the feet and spreads over the legs, with dense infiltration, and always the lesions are distinctly hemorrhagic. Sometimes cysts form which look like bullae; they are compressible and can be made to disappear by pressure but recur when the pressure is relieved. The lesions in this case have not been examined histologically, but clinically there is little to suggest Kaposi's sarcoma. The clinical appearance is that of nevocarcinoma.

Dr. M. H. Ebert: In the literature attention has been directed to the fact that many cases of Kaposi's sarcoma occur among Italians. Last night I glanced through the Archives of Dermatology and Syphilology, and every case of Kaposi's sarcoma that I found reported had occurred in an Italian. This is a rare disease which has a predilection for certain nationalities. The fact that this patient is a woman is against a diagnosis of Kaposi's sarcoma, as is the fact that there is no diffuse or brawny infiltrate, but I think that some of the early lesions look hemorrhagic. The patient has evidences of lesions on the other leg. The lesions are not so hemorrhagic today, as she has been in bed for several days. I shall be interested to see what the biopsy shows and will append the report.

Note.—Biopsy showed changes characteristic of melanocarcinoma.

DARIER'S DISEASE. Presented by DR. M. H. EBERT for DR. B. B. BEESON.

This man, aged 44, cannot give the exact duration of his disorder but states that it has been present for a few months. Lesions are present in the sites of predilection of seborrhea—about the ears, over the spinal column, about the genitalia and on the backs of the hands.

The lesions vary in size from that of a pinhead to that of a small pea. They are brownish papules with firmly adherent crusts. There are slight subjective symptoms.

Biopsy revealed the characteristic changes of Darier's disease.

Books Received

ANNUAL REPORT OF THE INSTITUTE FOR MEDICAL RESEARCH, FOR THE YEAR 1932. By A. Neave Kingsbury, Director, Institute for Medical Research, Kuala Lumpur, Federated Malay States, 1933.

L'ÉVOLUTION DE LA LUTTE CONTRE LA SYPHILIS: UN BILAN DE 25 ANS. By Louis Spillmann. Price, 30 francs. Pp. 292. Paris: Masson & Cie, 1933.

Directory of Dermatologic Societies *

FOREIGN

British Association of Dermatology and Syphilology (Canadian Branch)

Alberic Marin, President, Drummond Medical Bldg., Montreal.
Antonio Sabetta, Secretary-Treasurer, 3435 St. Denis St., Montreal.
Place: Hamilton, Ontario. Time: 1934.

Royal Society of Medicine, Section of Dermatology

A. M. H. Gray, President, 30 New Cavendish St., W. 1, London.
W. N. Goldsmith, Secretary, 6, Upper Wimpole St., W. 1, London.

NATIONAL DERMATOLOGIC SOCIETIES

American Medical Association, Scientific Assembly, Section on Dermatology and Syphilology

C. Guy Lane, Chairman, 416 Marlboro St., Boston.
Harry R. Foerster, Secretary, 208 E. Wisconsin Ave., Milwaukee.
Place: Cleveland. Time: June 11-15, 1934.

American Dermatological Association

Harold N. Cole, President, 1422 Euclid Ave., Cleveland.
W. H. Guy, Secretary, 500 Penn Ave., Pittsburgh.
Place: New York. Time: June 7-9, 1934.

SECTIONAL DERMATOLOGIC SOCIETIES

Baltimore-Washington Dermatological Society

Harry F. Anderson, President, 1610, 20th St. N.W., Washington, D. C.
Joseph V. Kennedy, Secretary, 1835 Eye St., Washington, D. C.

Central States Dermatological Association

Joseph Brumberg, President, 528 Delaware Ave., Buffalo.
William F. Hoover, Secretary, 333 Linwood Ave., Buffalo.
Place: Buffalo. Time: 1934.

Iowa and Western Illinois Dermatological Association

J. C. Kessler, President, University Hospital, Iowa City.
Robert E. Jameson, Secretary, 1014 First National Bank Bldg., Davenport, Iowa.

New England Dermatological Society

Rudolph Jacoby, President, 270 Commonwealth Ave., Boston.
J. Harper Blaisdell, Secretary, 5 Bay State Road, Boston.
Place: Boston. Time: April 11, 1934.

Southern Medical Association, Section on Dermatology and Syphilology

Thomas W. Murrell, Chairman, 17 E. Grace St., Richmond, Va.
C. C. Dennie, Secretary, Professional Bldg., Kansas City, Mo.
Place: San Antonio, Texas. Time: November, 1934.

---

* Secretaries of dermatologic societies are requested to furnish the information necessary for the editor to make this list complete and to keep it up to date.

STATE DERMATOLOGIC SOCIETIES

Florida Society of Dermatology and Syphilology

Chairman for each meeting is elected from city in which meeting is held.
Elmo D. French, Secretary, 602 Huntington Bldg., Miami.
Place: Jacksonville. Time: July 2, 1934.

Louisiana Dermatological Society

J. A. Devron, President, 150 Baronne St., New Orleans.
M. T. Van Studdiford, Secretary-Treasurer, 912 Pere Marquette Bldg., New Orleans.

Medical Society of the State of New York, Section on Dermatology and Syphilology

George M. Fisher, Chairman, 264 Genesee St., Utica.
Frank Combes, Secretary, 80 W. 40th St., New York.

Medical Society of the State of Pennsylvania, Section on Dermatology

Herbert J. Smith, President, 3303 N. 17th St., Philadelphia.
Robert L. Gilman, Secretary, 1930 Chestnut St., Philadelphia.

Michigan State Medical Society, Section on Dermatology and Syphilology

Robert C. Jamieson, Chairman, 1551 Woodward Ave., Detroit.
A. R. Woodburne, Secretary, Grand Rapids Clinic, Grand Rapids.
Place: Battle Creek. Time: September, 1934.

Minnesota Dermatological Society

D. D. Turnacliff, President, 407 Medical Arts Bldg., Minneapolis.
L. H. Winer, Secretary, 522 Medical Arts Bldg., Minneapolis.
Time: First Wednesday in October, December, February and April.

Oklahoma Dermatological Association

W. A. Showman, President, 108 W. 6th St., Tulsa.
C. L. Brundage, Secretary, 505 Osler Bldg., Oklahoma City.

Texas Dermatological Society

Everett C. Fox, President, 1719 Pacific Ave., Dallas.
Everett R. Seale, Secretary, 1215 Walker Ave., Houston.

LOCAL DERMATOLOGIC SOCIETIES

Atlanta Dermatological Society

Francis G. Jones, President, 384 Peachtree St., Atlanta, Ga.
Charles A. Wilkins, Secretary, Medical Arts Bldg., Atlanta, Ga.

Bronx Dermatological Society

Samuel Feldman, Chairman, 1955 Grand Concourse, New York.
Henry Silver, Secretary, 290 West End Ave., New York.

Brooklyn Dermatological Society

Arthur Persky, President, 1750 Ocean Parkway, Brooklyn.
George F. Price, Secretary, 884 Lincoln Place, Brooklyn.
Time: Third Monday of each month except June, July, August and September.

Buffalo-Rochester Dermatological Society

Earl D. Osborne, President, 471 Delaware Ave., Buffalo.
Richard L. Saunders, Secretary, 333 Linwood Ave., Buffalo.

Chicago Dermatological Society

James H. Mitchell, President, 25 E. Washington St., Chicago.
Max S. Wien, Secretary, 104 S. Michigan Ave., Chicago.

Cincinnati Dermatological Society

Harry L. Claassen, President, Provident Bank Bldg., Cincinnati.
Raymond G. Senour, Secretary-Treasurer, 19 W. 7th St., Cincinnati.

Cleveland Dermatological Society

S. Littman, President, 10515 Carnegie Ave., Cleveland.
H. G. Miskjian, Secretary, 856 Rose Bldg., Cleveland.

Detroit Dermatological Society

H. L. Keim, President, 10 Witherell St., Detroit.
William G. Saunders, Secretary-Treasurer, 9203 Grand River Ave., Detroit.

Los Angeles Dermatological Society

Stanley O. Chambers, Chairman, 727 W. 7th St., Los Angeles.
Nelson P. Anderson, Secretary, 2007 Wilshire Blvd., Los Angeles.

Manhattan Dermatologic Society

Howard Fox, Chairman, 140 E. 54th St., New York.
Mihran B. Parounagian, Secretary, 126 E. 39th St., New York.

Montreal Dermatological Society

J. F. Burgess, President, Drummond Medical Bldg., Montreal, Canada.
B. Usher, Secretary-Treasurer, 1538 Sherbrooke St., W., Montreal, Canada.

New York Academy of Medicine, Section of Dermatology and Syphilis

Leo Spiegel, Chairman, 241 W. 100th St., New York.
Eugene F. Traub, Secretary, 140 E. 54th St., New York.

New York Dermatological Society

Edward R. Maloney, President, 853 7th Ave., New York.
R. H. Rulison, Secretary, 145 E. 54th St., New York.

Omaha Dermatological Society

Alfred Schalek, Chairman, 721 Medical Arts Bldg., Omaha.
Donald J. Wilson, Secretary, 1216 Medical Arts Bldg., Omaha.

Philadelphia Dermatological Society

Jacques P. Guequierre, Chairman, 1930 Chestnut St., Philadelphia.
Robert L. Gilman, Secretary, 1930 Chestnut St., Philadelphia.

Pittsburgh Dermatological Society

Frederick Amshel, Chairman, 3401 5th Ave., Pittsburgh.
Bernhard Goldmann, Secretary, Jenkin's Arcade, Pittsburgh.

St. Louis Dermatological Society

Richard S. Weiss, President, 3720 Washington Blvd., St. Louis.
M. F. Engman, Jr., Secretary-Treasurer, 3720 Washington Blvd., St. Louis.

San Francisco Dermatological Society

H. J. Templeton, President, 3115 Webster St., Oakland, Calif.
John M. Graves, Secretary, 909 Hyde St., San Francisco.

THE ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY is published by the American Medical Association to stimulate research and disseminate knowledge in these departments of medicine.

Manuscripts for publication, books for review, and communications relative to the editorial management should be sent to Dr. [illegible], Chief, 7 West Madison Street, Chicago, or to any other member of the Editorial Board. Communications regarding subscriptions, [illegible] should be addressed, ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY, American Medical Association, 535 North Dearborn Street, Chicago.

Articles are accepted for publication on the condition that [illegible] solely to the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY. [illegible] be typewritten, preferably double-spaced, and the original [illegible] Zinc etchings and halftone illustrations will be [illegible] when the original illustrations are sent.

Footnotes and bibliographies should conform to the style of the Cumulative Index Medicus, published by the American Medical Association, and requires, in order given: name of author, title of article, [illegible] volume, page, month — day of month if weekly — and year.

Matter appearing in the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY is not covered by copyright, but, as a courtesy, no objection will be made to its use in reputable medical journals if proper credit is given. [illegible] duction for commercial purposes of articles appearing in the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY, or of any of the other publications issued by the Association, will not be countenanced.

Authors will receive [illegible] reprints; additional [illegible] obtained at cost.

The ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY is published monthly. Annual subscription price (two volumes): Domestic, $8.00; Canadian, $8.40; foreign, $9.00, including postage. Single copies, 85 cents.

Checks, etc., should be made payable to the AMERICAN MEDICAL ASSOCIATION.

OTHER PERIODICAL PUBLICATIONS
of the American Medical Association

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION—Weekly. [illegible] medical sciences and matters of interest to the medical profession. Illustrated. Annual price (two volumes): Domestic, $8.00; Canadian, $8.40; foreign, $9.00.

ARCHIVES OF INTERNAL MEDICINE—Monthly. Devoted to the [illegible] original clinical and laboratory contributions to internal medicine. Annual subscription price (two volumes): Domestic, $8.00; Canadian, $8.40; foreign, $9.00. Single copies, 75 cents.

ARCHIVES OF NEUROLOGY AND PSYCHIATRY—Monthly. [illegible] tion of original articles on neurology and mental diseases, with abstracts from foreign and domestic literature, book reviews, the transactions of societies, etc. Illustrated. Annual price (two volumes): Domestic, $8.00; Canadian, $8.40; foreign, $9.00.

AMERICAN JOURNAL OF DISEASES OF CHILDREN—Monthly. [illegible] a medical science and as a specialty. It includes carefully [illegible] based on recent pediatric literature, abstracts from foreign and domestic reviews, current transactions of societies, annual [illegible] Annual price (two volumes): Domestic, $8.00; Canadian, $8.40; foreign, $9.00. Single copies, 85 cents.

ARCHIVES OF SURGERY—Monthly. Devoted largely to the [illegible] phases of surgery, with monthly [illegible] on orthopedic and urologic surgery. Annual subscription price (two volumes): Domestic, $8.00; Canadian, $8.40; foreign, $9.00. Single copies, 85 cents.

ARCHIVES OF OTOLARYNGOLOGY—Monthly. A medium for [illegible] articles on diseases of the ear, nose and throat, with abstracts from [illegible] cure, book reviews, the transactions of special societies, etc. Illustrated. Annual price (two volumes): Domestic, $8.00; Canadian, $8.40; foreign, $9.00.

ARCHIVES OF PATHOLOGY—Monthly. A periodical [illegible] original contributions in the field of pathology, with abstracts [illegible] ture, book reviews, the transactions of special societies, etc. Illustrated. Annual price (two volumes): Domestic, $8.00; Canadian, $8.40; foreign, $9.00.

ARCHIVES OF OPHTHALMOLOGY—Monthly. Includes original [illegible] eye, abstracts from foreign and domestic literature, book reviews, transactions of societies, etc. Illustrated. Annual subscription price (two volumes): Domestic, $8.00; Canadian, $8.40; foreign, $9.00. Single copies, 85 cents.

QUARTERLY CUMULATIVE INDEX MEDICUS—Classified [illegible] author index to the worth-while medical literature of the world. Annual subscription price: Domestic, $12.00; Canadian, $12.60; foreign, $13.00. Second and fourth volumes contain [illegible] for permanent reference. Annual subscription price: Domestic, $12.00; Canadian, $12.60; foreign, $13.00.

AMERICAN MEDICAL ASSOCIATION
535 North Dearborn St. CHICAGO